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JOURNAL OF GERONTOLOGY

VOLUME 15, NUMBER 1
JANUARY, 1960

Section A

Biological Sciences and Clinical Medicine

JOURNAL OF GERONTOLOGY

VOLUME 15, SECTION A JANUARY, 1960 NUMBER 1

THE EXPERIMENTAL PRODUCTION OF SENILE PIGMENTS IN THE NERVE CELLS OF YOUNG RATS*

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Pigmentation of nerve cells is generally associated with senility; in fact the lipofuscin pigment is usually called senility pigment. Dolley and Guthrie (3) in reviewing the literature point to numerous early investigations and opinions concerning the role that pigmentation plays in aging.

Schäfer (13) presented the view that pigmentation can be interpreted as a sign of functional activity rather than decadence, since pigments were much more abundant in nerve cells of adults than in the nerve cells of children and lower animals. Hodge's (7) studies led him to conclude that pigmentation of nerve cells was related to senility. He observed that the cytoplasm of nerve cells from senile human individuals was largely filled with pigment, whereas the nerve cells of the fetus contained almost no pigment. White (24) concluded that the accumulation of pigment in the nerve cell of autonomic ganglia was due to loss of function. He showed that pigment in nerve cells decreased as the mammalian scale is descended until it is no longer observed. Therefore, he postulated that the autonomic ganglia become less and less important as the animal scale is ascended until its minimum of importance is reached in man.

Dolley (2) observed that while pigment is associated with senility, it is because "in the duality of senility, i.e., senility of function and senility of depression, the factor of depression is almost inevitable in an organism."

A number of studies have been made on the characteristics and nature of the pigment in autonomic ganglion cells. Kuntz (9, 10) agreed with the majority of the early investigators as to the dual nature of the pigment. He found that the pigments in autonomic cells were of two kinds. One he identified as a yellow pigment, which reacts to fat stains and which is at least partially soluble in alcohol, ether, and other fat solvents. He described the other as a darker, more stable pigment, which did not react to fat stains and which was highly insoluble. This darker pigment was referred to as melanin. Spiegel and Adolf (15) further described this dark pigment (melanin) as arising from the yellow pigment. With advancing age, the yellow pigment commonly disappears, leaving only dark pigment in a majority of the autonomic ganglion cells. Truex (21) also concurred with the presence of melanotic pigment in autonomic nerve cells of persons of all ages.

Sympathetic ganglion cells containing both melanin and lipochrome pigments were described by Larsell (11). His work also supported the reports by Strong and Elwyn (16) that the lipochrome pigment was not present in nerve cells at birth but was found in increased amount with age.

Wolf and Pappenheimer (25) in their work on the nerve cell suggest that a chemical relationship exists between the pigment they described and the substance called ceroid reported by Lillie, Daft, and Sebrell (12) in their studies on livers of vitamin E-deficient rats. They also report that in their study of the dorsal sensory ganglia this pigment is present in addition to melanin but never in the same cell.

Sulkin (17) has further attempted to characterize the nature of pigment in autonomic nerve cells with the use of histochemical methods. He has observed pigmented ganglion cells in individuals ranging in age from 7 to 92 years. The data obtained as a result of his studies in-

* This investigation was supported in part by Research Grant B-342, from the National Institute of Neurological Diseases and Blindness, Public Health Service.

dicated that there were no melanotic pigments in human autonomic ganglion cells. No evidence was obtained, moreover, to support the view that lipid-containing pigments could be transformed into melanin. A comparison of pigment in autonomic ganglion cells and in human cirrhotic livers indicated that they have similar properties, which are both similar to the properties of ceroid. Later studies on the pigments of sensory ganglion cells, ventral horn cells, and Purkinje cells (18) showed similar results to those obtained with autonomic ganglion cells. D'Angelo, Issidorides, and Shanklin (1) studying the staining reactions of granules in the human neuron have confirmed these observations. On the basis of their findings, they agree with the writer that the pigment granules are similar to ceroid as well as to the vitamin E-deficient pigment.

There is no conclusive evidence to indicate whether pigmentation of nerve cells is due to an intrinsic factor of aging or whether the pigment is accumulated in the cell because of extrinsic environmental factors in which the factor of aging is coincidental. There is some support for the latter point of view. In experimental laboratory animals, where the environment is to some degree controlled, pigments do not accumulate in the nerve cell until the animal is senile. Even at this time, the deposition of pigment is not marked. In the dog, where the environment is controlled to a lesser degree, deposition of pigments in nerve cells again does not occur prior to old age. However, the accumulation of pigment in the senile dog is much greater than it is in the laboratory animal. In man, where the environment is even less controlled, the nerve cells are characterized by the presence of pigments in almost all age groups. The concentration of pigment varies markedly in different individuals irrespective of their age groups.

The present study has been designed to determine the possibility of producing pigments in the nerve cells of young rats by altering the environment so that data could be obtained concerning the role of extrinsic factors in the deposition of nerve cell pigments.

MATERIAL AND METHODS

The lipofuscin pigments in these experiments were visualized by the PAS technique following diastase digestion, which removed the glycogen. It has been demonstrated, however, that PAS positive mucoprotein granules occur in the cytoplasm of many neurons in various species (18, 19, 20). In order to distinguish the lipofuscin pigment from the mucoprotein granules, alternating sections were stained with Sudan black, oxidized with performic or peracetic acid prior to staining with the Schiff reagent, stained for acid fastness, and treated by the Schmorl (14) ferri-ferricyanide reduction test.

The following experiments were performed:

A. *Acetanilid experiments.*—Thirty-six young rats, 2 to 3 months of age, were given 3.7 mg./Kg. of acetanilid daily, by tubal administration for periods up to 90 days. At the end of 90 days, 18 of the animals were sacrificed, and the administration of acetanilid was discontinued in the remaining 18 rats. At the time of sacrifice of the animals, the brain, superior cervical ganglia, spinal ganglia, and spinal cord were removed, fixed in 10% formalin, dehydrated, embedded in paraffin, and sectioned in the routine manner. Successive sections from each tissue were treated with the PAS technique and with the other methods mentioned above.

The remaining 18 rats were placed on a diet of stock laboratory chow and were sacrificed at varying intervals in a period of from 6 months to 18 months following the cessation of the administration of the acetanilid.

B. *Hypoxic chamber experiments.*—Twenty young rats were placed in an anoxic chamber in which the amounts of oxygen and nitrogen that were introduced could be regulated. The oxygen level within the chamber was measured by means of an oxygen analyzer. The oxygen and nitrogen were controlled so that there was a gradual diminution of the former. From the fifth day to the twenty-first day the level of oxygen was maintained at from 5% to 8.9%. The 8 animals which were still alive at the end of the 21st day were sacrificed, the nerve tissues were removed, fixed in formalin, and processed according to the manner described above.

C. *Vitamin E-deficiency experiments.*—One hundred and ten rats, from 6 weeks to 3 months of age, were placed on a vitamin E-deficient diet for periods up to 600 days. This diet had the following composition: 20% vitamin-free test casein GBI, 56% dextrose, 10% lard, 4% salt mixture (8), 10% brewer's yeast powder, together with the following fat-soluble vitamins per 100 pounds: 523 Gm. cod liver oil or 68 Gm. carotene in oil, GBI type 3a, and 0.001 Gm. calciferol. The rats were sacrificed at varying time intervals after being maintained on

this diet 150 days or more and kept on a stock laboratory diet for 90 to 400 days before being sacrificed.

D. *ACTH experiments.*—Twenty-four rats, including 12 rats 4 months of age, 6 rats 8 months of age, and 6 rats 27 months of age, were separated into 3 groups. The first group served as controls. The second group underwent a unilateral nephrectomy. The third group was subjected to a unilateral nephrectomy, after which each animal received subcutaneous injection of 0.33 unit of ACTH gel per 100 Gm. of body weight every other day for 48 days beginning 10 days after the unilateral nephrectomy. The brains, spinal cords, autonomic ganglia, and sensory ganglia were dissected out, following fixation by perfusion, and were processed as described above.

The rats that were used in the acetanilid experiments and in the chronic anoxia experiments were of the Wistar (MW-2) strain. The vitamin E-deficiency experiments were performed on rats of the Wistar (MW-2), the C. F. Nelson, the HLA, the Long-Evans, and the Sherman strains. The rats which were subjected to unilateral nephrectomy and ACTH administration were of the C. F. Nelson strain.

RESULTS

A. *Acetanilid experiments.*—It is well known that the excessive or long continued use of certain nitrogen-containing compounds, particularly acetanilid, results in the formation of methemoglobin in the blood. This, in turn, could result in a condition of chronic anoxia.

It was noted that after three weeks of daily tubal administration of acetanilid the animals became extremely lethargic. Upon autopsy it was observed that all of the animals suffered from cranial subdural hemorrhages and clots. In some instances, subdural hemorrhages were noted in the spinal cord.

Examination of the blood showed a variation in the hematocrit from 32% to 54%, with a mean hematocrit of 48.5% as compared with an hematocrit of 39% in control animals. The hemoglobin (Haden-Hauser Scale) ranged from 10 to 13 Gm.% with a mean of 11.3 Gm.% as compared to a reading of 15.6 Gm.% in the control animals. Determination of methemoglobin by the microphotometric method of Evelyn and Malloy (6) in the experimental rats indicated a methemoglobin concentration of just below 50%.

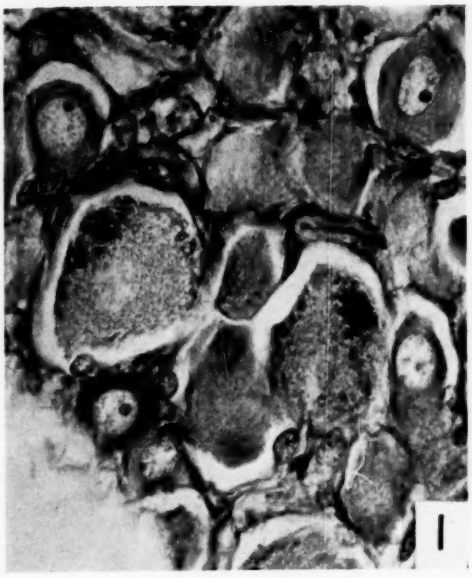
In the group of animals which were sacrificed at intervals from 3 weeks to 40 days after the initiation of the experiment there was no indication of pigment deposition. The group which was sacrificed at varying intervals from 45 days to 90 days following the beginning of the experiment, on the other hand, was characterized by a deposition of lipofuscin in the cytoplasm of nerve cells from autonomic ganglia, sensory ganglia, ventral horn cells of the spinal cord, Purkinje cells, and from neurons in various areas of the brain (fig. 1). Control animals of the same age showed no indication of neuronal lipofuscin pigment.

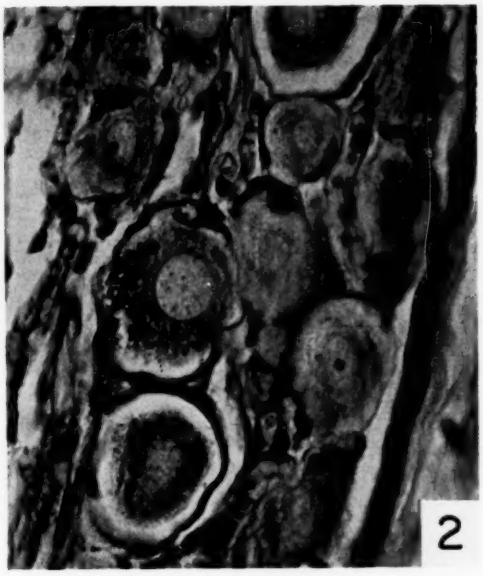
In the remaining rats, which were sacrificed at various intervals in a period of 6 months to 18 months following the cessation of the administration of the drug, the lipofuscin pigment in the cytoplasm of the nerve cells occurred with a similar distribution and concentration as observed in the previous group (fig. 2).

In an ancillary experiment, 3 young dogs, including 1 dog 3 months old and 2 dogs approximately 6 months old, were given capsules containing, respectively, 24, 45, and 60 mg. of acetanilid daily for a period of 77 days. At the end of this period the nerve tissue which was removed, including specimens of all parts of the nervous system, was characterized by the presence of lipofuscin pigment in the cytoplasm of many of the nerve cells. In the normal, well-cared for dog, such pigment is usually not observed until the animal reaches an age of approximately 9 years.

B. *Hypoxic chamber experiment.*—Following the conditions described in the experiment, the animals that remained alive after 21 days were sacrificed and the various parts of the nervous system were dissected and processed. Numerous nerve cells from different parts of the nervous system of all of these animals were characterized by the presence of lipofuscin pigment in the cytoplasm (fig. 3).

C. *Vitamin E-deficiency experiments.*—In each instance in which the animals had been subjected to the vitamin E-deficient diet for 150 days or more, the cytoplasm of the nerve cells from various parts of the nervous system was characterized by large deposition of lipofuscin pigment (figs. 4, 5). The concentration of pigment was greater in the vitamin E-deficient animals than in the animals subjected to the other experimental procedures. Moreover, the concentration of this pigment was greater than





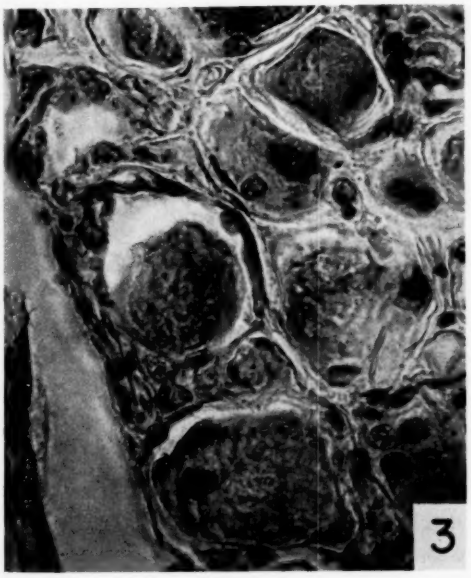
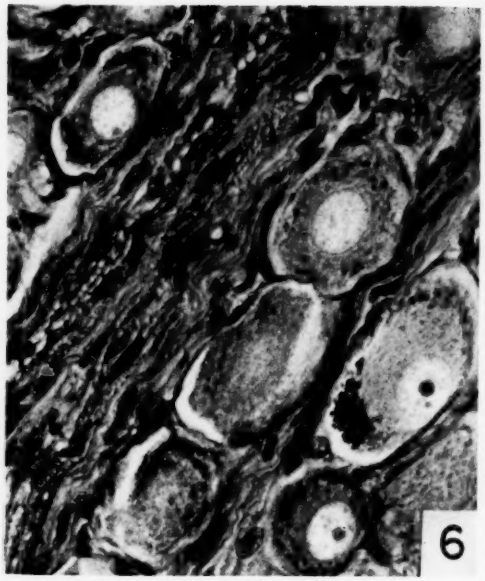


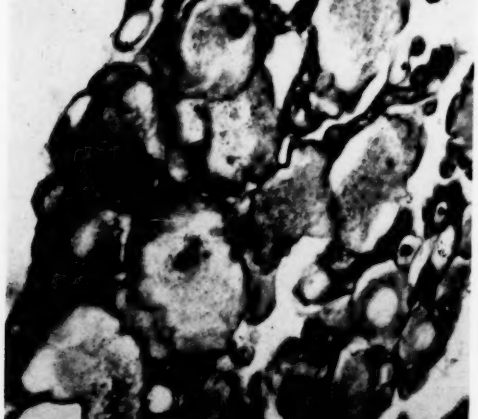
Fig. 1. Photomicrograph from section of spinal ganglion from young rat maintained on a daily supplement of acetanilid for 90 days, colored by the PAS reaction. 10X ocular, 48X objective.

Fig. 2. Photomicrograph from section of spinal ganglion from a rat which had been maintained on a stock diet for 8 months after cessation of the administration of acetanilid, colored by the PAS reaction. 10X ocular 48X objective.

Fig. 3. Photomicrograph from section of spinal ganglion from young rat subjected to low oxygen tension for 21 days, stained with Sudan black. 10X ocular, 48X objective.

Fig. 4. Photomicrograph from section of spinal ganglion of rat maintained on a vitamin E-deficient diet for 245 days, stained with Sudan black. 10X ocular, 48X objective.





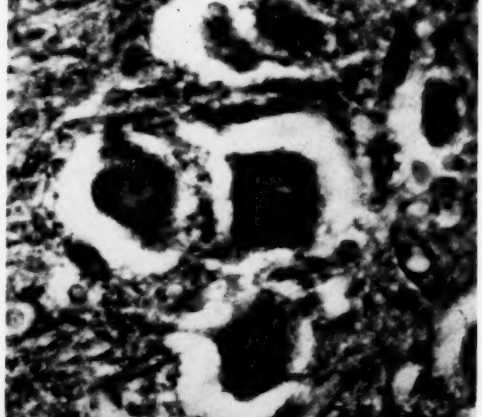


Fig. 5. Photomicrograph from section of spinal cord from young rat maintained on a vitamin E-deficient diet for 290 days, colored with the PAS reaction. 10X ocular, 48X objective.

Fig. 6. Photomicrograph from section of spinal ganglion of rat which had been maintained on a stock diet for 75 days after having been subjected to a vitamin E-deficient diet for 230 days, colored with the PAS reaction. 10X ocular, 48X objective.

Fig. 7. Photomicrograph from section of spinal ganglion from 4-month-old female rat treated with ACTH for 48 days following unilateral nephrectomy, colored with the PAS reaction. 10X ocular, 48X objective.

Fig. 8. Photomicrograph from section of spinal cord from 4-month-old female rat treated with ACTH for 48 days following unilateral nephrectomy, colored with the PAS reaction. 10X ocular, 48X objective.

is observed in the neurones of senile rats; even in rats which were only 210 days old at the termination of this experiment.

Some animals were removed from the vitamin E-deficient diet at various intervals after 150 days and were placed on the stock laboratory diet. In all such instances, the pigment was retained in the nerve cells even after intervals of more than 18 months (fig. 6).

D. *ACTH experiments.*—The control animals in the 4-month-old group of rats showed no indication of the deposition of lipofuscin pigments in nerve cells of any part of the nervous system which was examined. The rats of this age group which were examined 58 days following unilateral nephrectomy were characterized by the presence of small amounts of lipofuscin pigment in the cytoplasm of a few scattered nerve cells in various portions of the nervous system. The ACTH-treated rats of this age group showed significant amounts of lipofuscin pigment in the cytoplasm of numerous nerve cells in all parts of the nervous system (figs. 7, 8).

In the normal rats of the 8-month-old group, occasional cells in various parts of the nervous system showed lipofuscin pigment in the cytoplasm. The rats of this age group which had been subjected to unilateral nephrectomy and to unilateral nephrectomy together with the administration of ACTH were similar in regard to the pigment distribution to the 4-month-old groups which had undergone similar treatments.

The cytoplasm of numerous nerve cells in the 27-month-old series of normal rats contained depositions of lipofuscin pigment. This was particularly noticeable in autonomic ganglion cells, sensory ganglion cells, ventral horn cells, Purkinje cells, and cells of the pontine nuclei, although the pigments were also observed in other portions of the central nervous system. In relation to their pigment content, the nerve cells of the rats in this age group which had been subjected to unilateral nephrectomy could not be distinguished from the control group of senile animals. On the other hand, in the animals of this age group which had received ACTH, the cytoplasm of most of the nerve cells were characterized by large amounts of pigment. The amount of pigment was present in much greater concentration than is normally found in the nerve cells of senile rats and was comparable in amount to that which is present in nerve cells of vitamin E-deficient rats.

The latter group of experiments as well as the preceding experiment indicated that the sex of the animal did not seem to be concerned in the process of pigment deposition.

DISCUSSION

The data obtained in this study present evidence which supports the view that the production of lipofuscin pigments in nerve cells may be brought about by extrinsic factors, such as environmental alterations, which are not related to the factor of aging. It further presents data which indicate that the production of pigment is a non-reversible phenomenon, that is, under the conditions of these experiments the pigment produced in nerve cells remains in the nerve cell indefinitely.

The determination of the production of chronic anoxia in the young animals by the administration of acetanilid was considered outside of the scope of the present studies. Although the deposition of pigment in the nerve cells resulted from such administration of the drug, it is not known whether this phenomenon was brought about by a lowering of the oxygen content, by a direct action of the acetanilid, the subdural hemorrhages, and their consequent effects, or as a result of other factors. The significance of this experiment was the demonstration that deposition of the so-called senile pigment could be initiated by experimentally altering the environment.

The occurrence or degree of anoxia, not having been determined in the above experiment, suggested the feasibility of constructing an anoxic cage which would enable us to have precise information concerning the oxygen environment of the animals. As has been demonstrated, the lowering of the oxygen level in the environment also resulted in the deposition of pigment in the nerve cells of young rats.

The deposition of lipoid products in the nervous system of vitamin E-deficient rats was first described by Einarson and Ringsted (4). Later, Einarson (5) further characterized this substance. The properties of this lipoidal substance are identical to the properties of the so-called senility pigment (17). Einarson's studies, as well as subsequent studies of other workers, were made on adult rats or without knowledge of the age of the animal. Since older rats are characterized by the presence of pigment in the nerve cells even in ordinary nutritive states, the present studies were performed on groups of rats

which included very young animals. It has been demonstrated that a chronic vitamin E-deficiency, even in the youngest groups of animals, results in a deposition of lipofuscin pigment in the cytoplasm of the nerve cells. It is of further interest to note that vitamin E-deficiency results in a greater degree of pigmentation than is found following the other experimental procedures on the senile rats, even those between 1500 and 1600 days of age.

Wexler and Miller (22, 23) have suggested that excess pituitary-adrenal activity deserves further investigation as a possible mediator of the aging process and that exogenous ACTH may cause premature aging. Although it has been demonstrated in the present study that the administration of exogenous ACTH results in the deposition of senile pigments in the nerve cells of the young rat, there is no reason to believe that this procedure was responsible for the production of a premature aging. It is suggested, instead, that the deposition of the pigment was initiated by factors resulting from the stress associated with the increased ACTH rather than by a factor of premature aging. To support this view it is pointed out in these experiments that unilateral nephrectomy without ACTH administration apparently caused sufficient stress to produce pigments in the nerve cells of young rats and to increase the amount of pigment in in the nerve cells of older animals.

The data derived from these studies suggest the possibility that natural phenomena or alterations in the environment, including disease, nutritional deficiences, and emotional and physical stresses, could be considered as factors which initiate the deposition of lipofuscin pigments in nerve cells. It would not be unreasonable to assume that senile organisms are more susceptible to such factors. It is further suggested that the increased amount of pigment often observed in older individuals may represent an accumulation of such pigment during the life span.

SUMMARY

Thirty-six young rats, 2 to 3 months of age, when subjected to daily tubal administration of acetanilid for periods from 45 to 90 days are characterized by a deposition of lipofuscin pigments in the cytoplasm of their nerve cells. A discontinuance of the administration of the drug for periods of up to 18 months resulted in the continued presence of the pigment in the cytoplasm of these cells.

The occurrence of lipofuscin granules in the cytoplasm of nerve cells in 8 young rats was observed following the subjection of these animals to a lowered oxygen tension within an anoxic cage for a period of 15 days.

One hundred and ten young rats were maintained on a vitamin E-deficient diet for periods of 150 days to 600 days. Nerve cells in all of these rats were characterized by the presence of large amounts of lipofuscin pigment in the cytoplasm. Removal of the animals from this vitamin E-deficient diet for prolonged periods did not alter the occurrence and distribution of this pigment.

Twenty-four rats in different age groups, subjected to ACTH administration for a prolonged period of time following unilateral nephrectomy, were also characterized by either the occurrence or by an increase in the amount of lipofuscin pigment in the cytoplasm of the nerve cells.

It is suggested, as a result of the data obtained here, that senile pigmentation of nerve cells may be due to extrinsic factors rather than an aging factor.

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AGING OF HUMAN COLLAGEN IN RELATION TO SUSCEPTIBILITY TO THE ACTION OF COLLAGENASE*

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Previous studies (4, 5) have shown that human collagen loses its osmotic swelling ability and ability to swell at elevated temperature with advancing age. These findings were interpreted to mean that as collagen ages it passes through several stages of increasing rigidity. The mechanism by which such an increased rigidity might develop was hypothesized to be either thermal denaturation at body temperature or tanning of the collagen by physiological agents as proposed by Bjorksten (1). Both processes might lead to formation of new bonds between adjacent polypeptide chains of collagen. Heat treatment of young collagen caused an age-like loss of swelling ability, and thermodynamic calculations were consistent with the view that loss of swelling ability with advancing age was due to thermal denaturation (5). This view was given further support by the finding that both heat treatment and age resulted in decreases in the proportion of collagen which was soluble in acid and in the base-binding capacity of collagen (6).

The greater number of properties of collagen which are similarly affected by heat and aging, the greater the probability that aging of collagen is due to thermal denaturation. In considering additional properties of collagen to study in this regard, it seemed that an investigation of the effects of heat and aging on susceptibility of collagen to collagenase digestion would be informative. It had previously been reported by Keech (3) that human skin collagen became less susceptible to collagenase digestion with advancing age.

The present investigation was undertaken to discover if a similar age-related loss in digestibility occurred in human tendon collagen and if heat treatment resulted in age-like changes in digestibility. This study revealed that heat treatment did not cause age-like changes in digestibility, the latter apparently being the only property of human collagen studied in this regard which is not affected similarly by aging and by heat treatment.

The absence of a heat effect led to an investigation of the influence of tanning on digestibility because of the possibility that tanning *in vivo* is important in aging of collagen. From the studies of Bjorksten (1) it seemed likely that physiological tanning agents would contain aldehyde groups. Aldehydes might either diffuse into connective tissue over a long period of time or constituents of the collagen molecule might be converted to aldehydes by other physiological agents. It has been shown by Landucci and associates (7) that collagen normally contains aldehydes, among which are pyruvic acid and dihydroxyacetone. In addition, Gallop and associates (2) have reported that treatment of gelatin with hydrogen peroxide causes conversion of some of its constituents to formaldehyde. Thus, it is possible that formaldehyde is formed *in vivo* by the action of oxidizing agents on collagen. In the present investigation, collagen was treated with aldehydes to determine whether or not such treatment resulted in age-like changes in susceptibility to the action of collagenase.

MATERIALS AND METHODS

The source of collagen was the central tendon of the human diaphragm. Specimens comprising the young group were from 12 individuals under 30 years of age, while the old group was made up of 13 specimens over 60 years of age. According to previous studies (4, 5), changes in some physical properties of collagen occurred between 30 and 60 years of age. Thus this period would be expected to be one of transition in which measurements might be of equivocal significance.

Tendons were obtained from autopsies in which the diaphragm was not involved in any disease process. Pleural and peritoneal surfaces were removed, after which the remaining mat of collagen bundles was stored at −60 C. until used. Collagen was prepared for incubation with collagenase by mincing it while frozen and homogenizing the mince in mammalian Ring-

* This investigation was supported by a grant (H3123-C1) from the US Public Health Service.

† US Public Health Service Fellow in Pathology.

er's solution in a ground glass homogenizer at approximately 5 C. The resulting suspension was adjusted to yield a concentration of 20 mg. of tendon per ml. Since the concentration of collagen in tendon does not vary with age (5), the final suspensions contained about the same concentration of collagen regardless of the age of the specimens.

The collagenase preparation was obtained from a filtrate of a *Clostridium histolyticum* culture (Nutritional Biochemicals Corporation). It was used as an 0.1% solution in Ringer's solution adjusted to pH 7.4. The tendon suspensions were divided into 0.5 ml. aliquots. To these aliquots were added, in duplicate, 0.5 ml. portions of the enzyme preparation. Ringer's solution was added to control samples of the tendon suspension. The mixtures were then incubated at 37 C. Following incubation, the mixtures were centrifuged at 2200 r.p.m. with one ml. of Ringer's solution which was removed by aspiration. Precipitates were washed with one ml. of Ringer's solution which was removed by recentrifugation. Collagen in the precipitates was then determined by the hydroxyproline method of Neuman and Logan (8). Considering the amount of collagen in the control samples incubated with Ringer's solution as 100%, the percentage of collagen digested and solubilized by the enzyme was calculated.

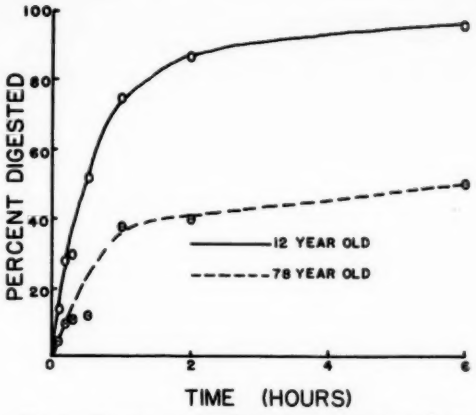

Fig. 1. Percentage of collagen in one young and one old sample digested as a function of duration of incubation with collagenase at 37 C.

RESULTS

Preliminary experiments were carried out to find appropriate times for incubation of collagen with collagenase. Results with one sam-

TABLE 1. PERCENTAGE OF COLLAGEN DIGESTED BY COLLAGENASE AS A FUNCTION OF AGE AND PRE-TREATMENT OF COLLAGEN.

Age, Years	No Treatment	Heated 56 C.	Formaldehyde	Dihydroxyacetone	Pyruvic Acid	Hydrogen Peroxide	Sodium Hydroxide	Sodium Hydroxide after Formaldehyde
1	93		16					
2	89	90						
5	86	90						
12	82							
21	78		0	75	80			0
21	88							
22	67					75		
26	81	69	0					11
28	64	66						
28	79							
28	64		0					1
29	76	80				87		
60	53							
61	33	34					83	
62	42		9				88	
63	39	31						
64	31						86	
65	27	30						
67	15	25						
68	28			27	36			
73	37		15					
78	25	35						
78	40							
79	39		0					
82	34		0					

ple of young collagen and one of old are shown in figure 1. It is apparent that a greater proportion of the young collagen than of the old was digested and that two hours' incubation was sufficient to demonstrate this age-related difference in digestibility. In all subsequent experiments collagen was incubated with collagenase for two hours. A series of 12 samples of collagen from young individuals and 13 from old individuals was then incubated with collagenase and the percentage of collagen digested in two hours was determined. The samples from young individuals were markedly and consistently more susceptible to the action of collagenase than the old specimens. The data from these determinations are included in table 1.

The effect of heating collagen on its subsequent digestibility was then investigated. Young collagen when heated at 56 C. underwent age-like changes in swelling ability, acid solubility, and base-binding capacity (5, 6). To find if heating caused an age-like decrease in susceptibility to collagenase, 5 young and 5 old tendon samples were heated in mammalian Ringer's solution for 20 minutes at 56 C. They were then cooled to room temperature, homogenized, and incubated with collagenase. Heat treatment did not decrease digestibility of collagen. Results of these experiments are included in table 1.

Attention was then directed toward the possibility that the loss in digestibility with age was due to tanning of collagen by physiological agents. To find if possible physiological tanning agents could cause an age-like decrease in digestibility of collagen, tendon fragments were incubated in 4% formaldehyde, 1 M pyruvic acid, and 1 M dihydroxyacetone for three hours at 37 C. Following incubation, the fragments were washed with large volumes of water, homogenized, re-washed with Ringer's solution, and finally incubated with collagenase. Extensive washing was necessary because minute traces of free formaldehyde destroyed the activity of collagenase.

To determine if collagenase activity was still present after the enzyme had been incubated with formaldehyde-treated collagen, the enzyme was removed by centrifugation and added to untreated collagen. It was found that if the formaldehyde-treated collagen was exhaustively washed, collagenase incubated with it for two hours retained full activity. As indicated in table 1, formaldehyde treatment markedly decreased the digestibility of collagen, while pyruvic acid and dihydroxyacetone had no effect on the susceptibility of collagen to collagenase activity. Control experiments in which collagen treated with aldehydes was incubated with Ringer's solution instead of collagenase indicated that aldehyde treatment had no effect on the determination of hydroxyproline in the collagen.

Young collagen was then incubated in 1 M hydrogen peroxide in Ringer's solution for one hour at 37 C., after which it was washed, homogenized, and incubated with collagenase. As formaldehyde treatment causes a decrease in digestibility of collagen and hydrogen peroxide causes the formation of formaldehyde in gelatin (2), it was anticipated that hydrogen peroxide treatment of collagen might result in decreased digestibility. Such an action of hydrogen peroxide might be analogous to a reaction between oxidizing agents and collagen *in vivo*. However, as shown in table 1, hydrogen peroxide did not cause an age-like loss in susceptibility of collagen to collagenase activity.

Landucci and associates (7) have pointed out that bonds between naturally occurring aldehydes and amino acids in collagen are weak and broken in formation of gelatin. An attempt was therefore made to break such bonds by alkali treatment of tendon which had lost susceptibility to collagenase activity through natural aging or by treatment with formaldehyde. Rupture of bonds by such treatment might result in increased digestibility of the young collagen type. Tendon fragments were incubated in 1 N sodium hydroxide for three hours at 37 C., after which they were washed and homogenized. The suspensions were adjusted to pH 7.4 and incubated with collagenase. Controls were treated with alkali but incubated with Ringer's solution instead of collagenase. As shown in table 1, alkali treatment caused old collagen to have the digestibility characteristic of young, but had no significant effect on formaldehyde treated young tendon.

DISCUSSION

The significance of this investigation is dependent on the demonstration that not all age-related changes in human collagen can be explained on the basis of thermal denaturation at body temperature. Regarding the digestibility of collagen, the data suggest that the decrease noted with advancing age may be due to a

chemical reaction between collagen and some metabolite functioning as a tanning agent.

The findings of the present study raised the possibility that in previous investigations in which heat treatment caused young collagen to assume the properties of old (5, 6), the collagen was actually reacting with some substance rather than simply undergoing thermal denaturation. This possibility led to a re-investigation of the effect of heat in causing collagen from young individuals to undergo an age-like loss in ability to swell at pH 2.5. Tendon fragments were exhaustively washed with Ringer's solution adjusted to pH 3, 7.4 and 10, after which they were heated at 56 C. After cooling to room temperature their swelling ability was compared with that of control fragments, which were neither washed nor heated, and with that of controls heated but not previously washed. It was found that washing did not influence the effect of heat on subsequent swelling ability. In addition, treatment of collagen with phenylhydrazine to block aldehyde groups prior to heating did not decrease the effect of heat on swelling ability.

These observations tend to negate the possibility that some diffusible substance or aldehyde present in tendon is responsible for the loss in swelling ability caused by heat treatment. The fact that heat treatment of young collagen did not result in loss of susceptibility to collagenase provides additional evidence that there is no tanning agent present in young tendon which will react with the collagen at an accelerated rate during heating.

The observations of this and previous studies can best be explained by the supposition that aging of human collagen occurs by at least two mechanisms. Since heat treatment *in vitro* causes age-like changes and it is known that collagen is exposed to body heat *in vivo* for long periods of time, it would be difficult to avoid the conclusion that thermal denaturation plays a role in aging of collagen. However, the findings of the present study necessitate the view that an additional chemical change occurs in aging collagen.

Possibly a tanning agent such as formaldehyde reacts with collagen *in vivo*, either following diffusion into connective tissue, or following conversion of some constituent of the collagen molecule to an aldehyde by an oxidizing agent. The latter is unlikely since hydrogen peroxide treatment did not influence digestibility of collagen. The observation that dihydroxyacetone and pyruvic acid were without effect would also tend to render it unlikely that such aldehydes occurring naturally in the collagen molecule influence digestibility.

The fact that sodium hydroxide treatment did not reverse the effect of formaldehyde tanning on digestibility casts some doubt on the view that age-changes in digestibility are due to simple tanning with an agent like formaldehyde. However, it is not known that sodium hydroxide caused old collagen to behave like young in regard to digestibility because of cleavage of bonds between collagen and a tanning agent. Further work is required to elucidate the mechanism by which formaldehyde and sodium hydroxide treatment influence the susceptibility of collagen to the action of collagenase.

The findings of this study incidentally indicate that in histochemical procedures employing collagenase, age and method of fixation of tissue will probably influence the extent of digestion. This investigation also raises the possibility that older individuals may be more resistant than young to tissue damage from infection by *Clostridium histolyticum*.

SUMMARY

This investigation was undertaken to discover if human tendon collagen varied in its susceptibility to the action of collagenase as a function of age, and if age-like changes could be produced by treating young collagen with heat or tanning agents. It was found that young collagen was more digestible by collagenase than old. Heat treatment did not influence digestibility, while formaldehyde tanning caused collagen to become less susceptible to collagenase activity.

Alkali treatment of old collagen caused it to assume digestibility characteristic of young material. It was concluded from this and previous studies that both thermal denaturation and a chemical reaction, possibly of a tanning type, may be of significance in aging of human collagen.

Note added in proof: After this paper was submitted it was found that resistance of formalin-fixed collagen to collagenase has previously been described (Keech, M. K.: The Effect of Collagenase on the Fixed and Unfixed Skin Lesions of Morphea: An Electron-Microscope Study. (*J. Path. Bact.*, 77: 351-369, 1959.)

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AGING AND THE LABILITY OF IRREPLACEABLE MOLECULES—II THE AMIDE GROUPS OF COLLAGEN*

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This paper deals with the question of the stability of the amide nitrogen of collagen and whether these amide groups persist for the lifetime of an organism.

Collagen is of particular interest in any discussion of aging because of its importance in the structure of blood vessels, bone, and skin, and because of the fact that its rate of replacement in adult organisms seems to be limited (7), thus giving opportunity for altered molecules to accumulate.

Cassel and McKenna (2) have described the hydrolysis of the amide nitrogen of hide powder at 100 C. and neutral pH. We attempted to use the Cassel and McKenna data to estimate the stability of collagen at 38 C. Reasonable assumptions could be made concerning the temperature dependence of this hydrolysis. If we assumed that the rate of amide hydrolysis doubled every 10 degrees, then the rate of hydrolysis at 38 C. would be approximately 2^{-6} or one sixty-fourth that at 100 C. Cassel and McKenna report that 21% of the amide nitrogen was released in 2 hours at 100 C. On this basis a similar amount would be released in 128 hours at 38 C. If the hydrolysis of amide groups occurred in collagen at even one-thousandth this rate, requiring 128,000 hours for 21% destruction or 15 years, the loss of amide groups from collagen with an accompanying increase in negative charge would become a significant factor in altering its properties with time.

It was apparent, however, that Cassel and McKenna's measurements were made on gelatin rather than collagen, since collagen is rapidly converted into gelatin at 100 C.

It seemed important to determine whether or not the spontaneous release of amide nitrogen occurred in collagen as well as gelatin.

EXPERIMENTAL

Strips of air-dried kangaroo tail tendon† were cut into 1.0-2.0 mm. pieces and weighed in ampules. The required amount of 0.1 M phosphate buffer, pH 7.35 (approximately 1 ml. buffer/20 mg. tendon), was placed in the ampules and the ampules were sealed. Tendons were allowed to presoak in this manner for an hour at room temperature. After treatment in a water bath for the specified time at elevated temperature, 1 ml. aliquots of the supernatant from each ampule were used to determine the amide nitrogen released as ammonia according to the standard diffusion technique described by Conway (3). Blank analyses were carried out on pieces of tendon which were placed in buffer and potassium carbonate in the Conway dishes without prior incubation.

The total amide nitrogen was determined by substituting 2.0 N HCl for buffer, and placing the ampules in a boiling water bath for three hours (2). The amide ammonia released was determined as before.

The total amide nitrogen of kangaroo tail tendon was found to be 3.28% of the total nitrogen, compared with 3.24% for rat tail tendon and 3.51% for ox tail tendon. We found 3.51% for the amide nitrogen of washed ox dermis in good agreement with the values given in the literature (1).

The release of amide nitrogen from gelatin seems to come from two pools of amide nitrogen, one of which is more labile than the other. This is illustrated in figure 1, on which the release of amide nitrogen from kangaroo tail tendon at 65.6 C. is plotted. It is apparent that the labile pool constitutes approximately 20% of the total amide. The release of amide nitrogen from this pool is approximately first order, as is shown on a logarithmic plot (fig. 2) assuming that the size of the labile pool is 20% of the total amide. From such plots the time for release of one-half of the labile amide may be calculated. In the case of the example this is 3 hours.

The results of our experiments are shown in table 1, which shows the time required for release of 50% of the labile amide and the time required for 50% thermal shrinkage.

* This work was supported by a grant (A-2066) from the National Institutes of Health.
We wish to acknowledge the very capable technical assistance of Miss Barbara Faris in carrying out these experiments.
† We are indebted to Johnson and Johnson Pty. Ltd. Sidney, Australia, for supplying this kangaroo tail tendon.

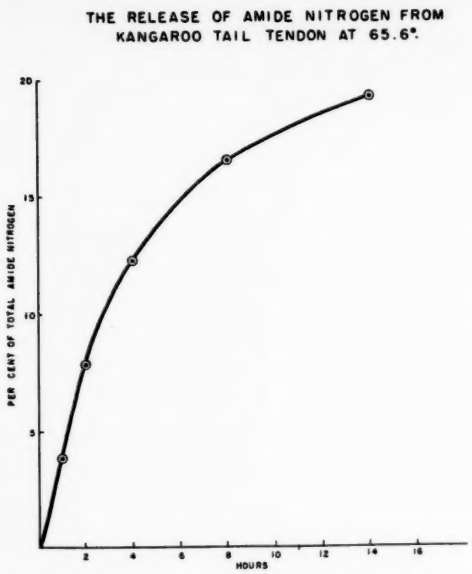

Fig. 1. The release of amide nitrogen from kangaroo tail tendon at 65.6 C. The percentage of total amide nitrogen is plotted against the time in hours.

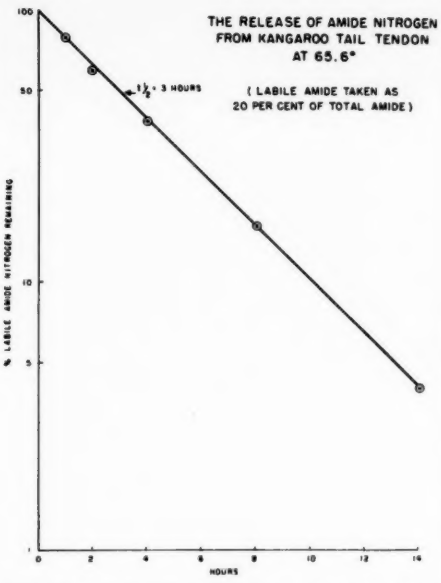
THE RELEASE OF AMIDE NITROGEN FROM KANGAROO TAIL TENDON AT 65.6°
(LABILE AMIDE TAKEN AS 20 PER CENT OF TOTAL AMIDE)
% LABILE AMIDE NITROGEN REMAINING
HOURS

Fig. 2. The release of amide nitrogen from kangaroo tail tendon at 65.6 C. The data shown in figure 1 have been plotted on a logarithmic plot, assuming that 20% of the amide is labile.

The values shown in table 1 were obtained by first estimating the time required for 50% release of amide nitrogen from a curve drawn through amide release values for 4 or 5 arbitrarily selected times. The apparent time required for 50% release was then confirmed by two additional experiments in which the anticipated 50% point was straddled by determinations in which duplicate samples were used. The standard deviation of determinations on a single sample of tendon is of the order of 25% due to variations in kangaroo tail tendon. The 8.1 sec. reported for 100 C. is probably slow due to the time required for the tendon strip and holder to come to temperature. The amide release reported for 45 C. is too fast for reasons which will be discussed.

The shrinkage of collagen has been treated as a phase transition by Florey and Garrett (4) and as an irreversible denaturation by Weir (8) and Sinex (6). In our experience the expression derived from the time required for one-half shrinkage can be plotted against the reciprocal of the absolute temperature, giving essentially a straight line as predicted by the theory of the activated state down to approximately 51 C. at which temperature the time required for one-half shrinkage for rat tail tendon is approximately 11 hours and for kangaroo tail tendon 44 hours. During prolonged incubation at lower temperatures, the tendon begins to soften and come apart, so that objective criteria of shrinkage become difficult to apply. We interpret these changes as due to dissolution of the material which binds together the fibrous matrix. This material, which one associates with the concept of ground substance, differs from collagen in presumably having a lower energy of activation for dissolution and

Table 1. The Release of Labile Amide Nitrogen from Kangaroo Tail Tendon.

Temperature C.	Minutes Required to Release 50% of Labile Amide	Time for 50% Shrinkage
100	8.1	Very fast
77	40	Very fast
65.6	180	16 seconds
60	290	4.3 minutes
45	3.6% in 2700 min†.	Several years?
65.6 for 5 min., then 45.	65% in 2700 min. ($t_{1/2}$ =1750 min.)	———

* Labile amide assumed to be 20% of total amide.
† For rat tail tendon this value is 5.2% in 2700 min.

in being replaced continuously during the lifetime of the organism.

At temperatures appreciably above the critical shrinkage temperature there is a rapid release of amide nitrogen. Below the critical shrinking temperature the release of amide nitrogen is slow. The labile amide nitrogens of collagen are stabilized in the collagen fiber but become labile when this semicrystalline structure becomes disorganized by thermal agitation. At temperatures above the critical shrinkage temperature the plot of the reaction rates as a function of temperature does not indicate an abnormally high entropy of activation characteristic of the shrinkage of collagen and the activation of large macromolecules, but rather is characteristic of the hydrolysis of simple amides. For example, between 60 and 65.6 C. the rate of shrinkage increased 16-fold while the rate of release of amide nitrogen increased 1.8-fold.

Additional evidence for the stabilization of amide nitrogen in native collagen is shown in the final experiments of table 1. In this experiment kangaroo tail tendon was incubated for 5 minutes at 65.6 C. (an interval sufficient for complete shrinkage, but which would give negligible amide release), and then at 45 C. for 2700 minutes. The amide release increased from 3.6% to 65%.

Examination of table 1 shows that a small amount of amide is released at 45 C. even if the collagen was not preshrunk. This was of considerable interest since 45 C. is fairly close to 38 C., body temperature for many organisms.

Unfortunately the significance of the release of small amounts of amide nitrogen from tendon is questionable, since control experiments carried out on more cellular tissues showed release of appreciable amounts of amide nitrogen under similar conditions. This is illustrated in table 2, which shows ammonia released when dried tissue is incubated at 45 C. More cellular tissues, such as liver and muscle, release substantial amounts of ammonia under these conditions. If 10% of the mass of the tendon had resembled muscle in this regard, an apparent release of 0.022 mg. of amide N might have been anticipated, which would represent 3.3% of the labile amide in 45 hours.

TABLE 2. APPARENT LABILE AMIDE OF RAT TISSUE.

Tissue	Mg. N/100 Mg. Dry Weight			
	45 C.		100 C.	
	24 hours	45 hours	15 min.	30 min
Tendon	.0032	.0053	.0748	.0815
Skin	.0330	.0364	.0368	.0543
Liver	.1168	.1204	.0351	.0520
Muscle	.2017	.2221	.0486	.0705

TABLE 3. PERCENTAGE OF TOTAL AMIDE NITROGEN RELEASED FROM TENDON AND BOVINE SERUM ALBUMIN AT 100 C.

Minutes	Tendon	Albumin
10	10.0	1.3
20	17.5	2.3
40	19.0	3.5

At more elevated temperatures this difference between tendon, skin, liver, and muscle is not apparent, as shown in the second column when the same tissues were incubated at 100 C. for 15 and 30 minutes. This indicates that the large release of ammonia at 45 C. is the result of enzymatic autolytic activity, and that the cellular elements of the tendon do not make an appreciable contribution to the release of ammonia at elevated temperatures.

Sterility was seldom a problem in the incubation of the tendon at 45 C. Control experiments on tendon in the presence of 50 units of penicillin and 50 micrograms of streptomycin per ml. did not affect values for amide nitrogen. Addition of nutrient broth and continued incubation at 45 C. did not lead to detectable growth. However, in experiments in which collagen was shrunk, prior to incubation at 45 C., there was considerable growth of microorganisms unless these quantities of penicillin and streptomycin were added.

It was of interest to compare the release of amide nitrogen from gelatin and a globular protein, such as bovine serum albumin. The results of this experiment are shown in table 3. It would seem that the amide groups of serum albumin are not of the labile type.

DISCUSSION

If the amides of collagen were as labile as those of gelatin, extrapolation of the data in table 1 would indicate that appreciable alteration in the properties of collagen would occur at 38 C. in a few days. However, it is apparent that the organization of the collagen molecule and collagen fiber makes these amide groups much more stable, although it is not apparent exactly how stable. This stabilization of amide nitrogen is an important property of collagen, since hydrolysis of these amide groups would

appreciably alter the charge on the surface of the collagen fiber, so important in determining its interaction with other substances and other collagen molecules. The semicrystalline state of collagen fibers may be considered in part an adaptation which confers extra stability to certain labile groups.

Any instability which remains might be a factor in aging and the alterations observed in blood vessels, skin, and bone of older individuals. According to Gustavson (5) a unit of collagen of 39,000 molecular weight contains approximately 31 free carboxyl groups and 33 free amino groups and is therefore essentially isoelectric at physiological pH. If 18 amides were removed, the balance of charge would shift to 49 carboxyl groups and 32 amino groups, which would give the surface of the fiber a definite negative charge.

One cannot determine from the data presented whether the stabilization of amide nitrogen in collagen is intramolecular or intermolecular. The thermodynamic evidence indicates only partial crystallinity in the fiber, so that protection of amides within the molecule may not be perfect. Furthermore, the amide groups on the exterior surface of the fiber might be less stable than those in the interior.

Unfortunately the really vital question of the long term stability of the amide nitrogens of collagen is not answered by the results of this study and must await more refined techniques.

The problem of evaluating the stability of amide nitrogen in other macromolecules is also difficult. Elastin, which resembles collagen in several respects, does not have the semicrystalline organization of collagen, and the spontaneous release of amide nitrogen from elastin might play a role in the deterioration of the internal elastic intima of blood vessels. Here the problem is how to prepare purified elastin for study without hydrolyzing more labile amide nitrogen.

Also challenging is the question of the state of amide nitrogens in other structures. Some of the same questions can be asked about the proteins of mitochondria, the proteins of genetic apparatus, of cell walls, and the surface of blood vessel endothelium.

SUMMARY

The stability of the amide nitrogen of collagen has been studied as a function of temperature. Certain amide groups in collagen became labile above the critical shrinkage temperature. It was not possible to evaluate the stability of these amide groups at 38 C., other than to indicate that they are much more stable below the critical shrinkage temperatures. The implications of instability in amide groups of collagen of other macromolecules are discussed.

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EXPERIMENTAL STUDIES ON BLOOD HYPERCHOLESTEROLEMIA IN RABBITS*

Evaluation of Age Influence and the Effect of Iodine Value and Carbon Number

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Surveys conducted after World War I and II in European countries and America (8, 12, 26, 27) were the first to point out the relationship between dietary fat and atherosclerosis. Numerous investigations have demonstrated that experimental cholesterolemia and atherosclerosis can be induced by feeding diets rich in cholesterol to monkeys (25, 37), dogs (35), rabbits (6, 10, 32, 33), chicks (13, 23), and rats (28, 29, 42).

It is generally agreed that diets low in fat decrease blood cholesterol levels, although this decrease does not always follow the same pattern in different individuals (41). Hypercholesterolemia is, as a rule, present in human atherosclerosis and gerontoxon (40). A moderate increase in total lipid values was demonstrable in about 50% of cases of arteriosclerosis without diabetes, while an increased cholesterol value was present in a smaller number of individuals (7, 32).

Dietary cholesterol seems to have little effect on elevating blood cholesterol levels in man (14, 15, 15). Accumulating evidence indicates that animal fats have an atherogenic property, while vegetable oils decrease blood cholesterol both in man and animals (1, 2, 3, 19, 20, 21); it was demonstrated that administration of sufficient quantities of certain vegetable oils resulted in a prompt fall of total lipids and cholesterol in blood of man and animals.

The influence of unsaturated fatty acids on blood cholesterol levels is not as yet determined. A diet rich in cholesterol and saturated fatty acids brought about a maximal hypercholesterolemia and the appearance of atherosclerosis both in rats and chicks (42). In rabbits, however, unsaturated fatty acids combined with cholesterol seemed to produce an increase in blood cholesterol levels (22). Clinical trials with vegetable oils of various degrees of unsaturation gave rather controversial results, which do not at the present time permit correlating the iodine value of a fatty acid with its anticholesterolemic property. Thus the opinion was expressed (39) that the degree of unsaturation is not the whole answer to the problem of hypercholesterolemia.

The problem of age influence on experimental and natural cholesterolemia and atheromatosis is of particular interest. Gram and Leverton (9) reported that serum cholesterol in women was increased from 177 mg./100 ml. serum in the group 17-25 years of age to 257.4 mg. in the group 60-70 years of age. Keys and associates (17, 18), on the basis of their survey of men of various ages, disclosed that younger men, 18-25 years of age, had a mean serum cholesterol level of 175-184, while the older group of men, 45-55 years of age, showed higher levels, 242-251. Lansing and associates (23) found progressive changes in aortal elastin of old rabbits which were absent in younger animals. Dauber (6) described arteriosclerotic lesions in 45% of chickens over one year of age, and Pollak (31) found that rabbits over one year of age are more susceptible to experimental atherosclerosis than younger rabbits. The elephant may exhibit atherosclerosis according to Chaikoff (5). Monkeys apparently do not develop this disease spontaneously, although some pathological changes in the aorta have been seen in baboons (11).

On the other hand, Sperry and Webb (34) concluded that hypercholesterolemia is not necessarily an attribute of aging. Having examined serum cholesterol levels of a group of their patients at the interval of 13-15 years, these investigators found no significant increase in blood cholesterol. In their opinion the variability of blood cholesterol levels is much less

* Aided by grants from the National Heart Institute, H-3232, and the Marcia Tucker Foundation, New York.

within a given individual than it is among individuals, and they offered the postulate that in each healthy person serum cholesterol concentration is maintained, perhaps throughout life, at a constitutional level, from which large deviations do not occur in the absence of unusual stress. As an interesting corrective to this postulate, the role of diet in longevity may be mentioned. As Thomasson (38) reported, the diet which accelerates the growth of rats resulted in shortening of their mean life span. Rats fed butterfat grew faster but lived a shorter time (545 days) than rats kept on rapeseed oil (669 days). Thus possibly not only constitutional factors but also eating habits to which an individual adheres are responsible for hypercholesterolemia of aging persons.

In the present study, the age influence on rabbit hypercholesterolemia and the role of unsaturation and carbon number of fatty acids on blood cholesterol levels were investigated, using a new method of three-day fasting.

MATERIAL AND METHODS

Cholesterol feeding.—Many investigators who described experimentally induced hypercholesterolemia in animals administered cholesterol in oil vehicles. The work of Swell and associates (36) and Wolff and Brignon (43) emphasized that intestinal absorption of cholesterol depends on the type of oil used as its vehicle. The higher the unsaturation of oil vehicles, the better was the assimilation of cholesterol with a corresponding increase of its blood levels. For this reason in all of the present tests in rabbits cholesterol was given orally in a form of water suspension.

Serum cholesterol determination.—The modified Liebermann-Burchard method (30) was used. Blood was taken from a rabbit ear vein after the animal had been fasting for 24 hours.

Three-day fasting method.—Wolff and Brignon (43) reported that a brief fasting method gave them reliable data on the anticholesterolemic properties of fatty acids, corresponding to those obtained by long-range assays. Accordingly, in this study a modified version of this method was employed for estimation of anticholesterolemic property of various oils and fatty acids, consisting of administering cholesterol three hours before a fatty acid was given and determining the blood cholesterol exactly 24 hours thereafter. The measurement was repeated on the second, third, and fourth days after the initial 24-hour fasting. The rabbits tolerated this regime well, and no casualties or ill-effects were observed. This method allows estimation of the anticholesterolemic activity of any compound without any other factors being involved. Cholesterol was administered in water suspension, 300 mg./Kg., and oils and fatty acids orally by a gastric tube, 2 ml./Kg. In the case of saturated fatty acids, a suspension in water was made before administration.

Material.—Fourteen types of fats, comprising fatty acids, vegetable oil fractions and fish oil fractions were employed in investigation of cholesterolemic effect of such compounds. The chemical characteristics of these preparations are described in table 4.

Estimation of iodine value.—The iodine value of every compound was checked according to the Official Method, A.C.C.S. Da 12-48, Section C.

EXPERIMENTAL

Influence of fasting on serum cholesterol levels.—Ten New Zealand male rabbits, average weight 1620 Gm. and average age 149 days, were placed on fasting. Six rabbits with approximately the same concentration of serum cholesterol after 24-hours' fasting were selected from the group. The rabbits received no food but were allowed to have water. Serum cholesterol was determined 24, 48, 72, and 96 hours after the onset of fasting. Table 1 summarizes the results of this experiment, and analysis of the data indicates that prolonged fasting tends to increase the serum cholesterol levels in rabbits.

Influence of age on serum cholesterol levels.—A group of 20 young male rabbits, average weight 923 Gm. and average age 42 days, were selected for this experiment. When their serum cholesterol concentrations were determined after 24-hours' fasting, considerable variation in cholesterol levels was found. Some rabbits had levels of 45-50 mg., while others had 110-120 mg./100 ml. serum. Accordingly, the rabbits were divided into three groups: Group I, 10 rabbits showing figures for cholesterol between 40-60 mg.; Group II, 4 rabbits between

TABLE 1. EFFECT OF FASTING ON SERUM CHOLESTEROL LEVELS IN RABBITS.

Number of Rabbits	After Fasting Period (Hours)			
	24	48	72	96
6	49.3 ± 2.5	56.5 ± 2.3	86.4 ± 3.3	76.4 ± 3.4

60-80 mg.; and Group III, 6 rabbits between 80-120 mg. The rabbits were kept on Purina rabbit ration, *ad libitum*, and their serum cholesterol was determined every 4 months.

The results of these experiments are presented in table 2. The rabbits of Group I and II showed no significant increase in serum cholesterol during one year of observation. The rabbits of Group III, however, with a higher serum cholesterol level at the age of 6 weeks, showed a definite trend toward elevation of their serum cholesterol. Their average weight was also increased more than in the two other groups. After one year of observation, the serum cholesterol levels went up about 36%. This assay might indicate that aging does not necessarily bring about spontaneous hypercholesterolemia and that some constitutional factors might be responsible for its development in some individuals.

Effect of cholesterol feeding on serum cholesterol levels.—Three groups of rabbits were used for this test. One group of 8 young male rabbits, average age 49 days, had approximately the same mean figure for their serum cholesterol concentration after 24-hours' fasting. The second group of 8 old male rabbits, average age 737 days, was selected from the old rabbit stock as showing no significant increase in their serum cholesterol levels during the three months of observation. The third group of 6 old male rabbits, average age 721 days, showed a definite trend toward moderate increase in serum cholesterol during the same period of time. Cholesterol, in water suspension, was administered by gastric tube, 300 mg./Kg. 24, 48, and 72 hours after the animals were placed on fasting. Serum cholesterol was determined each morning shortly before cholesterol administration 24, 48, 72, and 96 hours after the experiment was started. The results of these assays are presented in table 3.

There was no appreciable difference in the increase in serum cholesterol levels caused by cholesterol feeding between Group I and II. Both young and old rabbits responded in a similar manner by augmenting their serum cholesterol by about 230% after the 4-day fasting, but Group III, which was comprised of rabbits having a tendency to hypercholesterolemia, showed a much greater increase in serum cholesterol, 300%. The average serum cholesterol level of this group was as high as 325 mg./100 ml. Thus again there are apparently certain constitutional factors present in the rabbits of Group III which might account for

TABLE 2. AGE INFLUENCE ON SERUM CHOLESTEROL LEVELS IN RABBITS.

Groups and Number of Rabbits	Days of Observation			
	0	120	240	360
Group I 10 rabbits				
Cholesterol mg./100 ml.	48.3 ± 2.34	48.5 ± 2.96	51.2 ± 3.94	49.8 ± 3.34
Weight Average (Gm.)	912 ± 18			2842 ± 35
Age Average (Days)	42	162	282	402
Group II 4 rabbits				
Cholesterol mg./100 ml.	70.2 ± 3.45	68.2 ± 2.44	71.4 ± 3.55	69.6 ± 4.78
Weight Average (Gm.)	915 ± 15			2813 ± 39
Age Average (Days)	45	165	285	405
Group III 6 rabbits				
Cholesterol mg./100 ml.	102.0 ± 5.47	110.8 ± 2.35	128.8 ± 3.76	138.2 ± 4.74
Weight Average (Gm.)	917 ± 28			3123± 53
Age Average (Days)	40	160	280	400

the higher levels of serum cholesterol in this group.

Influence of iodine value and carbon number on serum cholesterol levels.—Fourteen saturated and unsaturated fatty acids and unsaturated fatty acid fractions from vegetable and fish oils were tested on rabbits, following the same fasting procedure. For each test 10 rabbits of the same age and sex, with approximately the same response to the initial cholesterol feeding, were used. Four of them served as controls, receiving only cholesterol, and 6 rabbits were given cholesterol, 300 mg./Kg. and fatty acid, 2 ml./Kg. for three consecutive days. Blood samples were taken early in the morning. Cholesterol, in water suspension, was administered soon thereafter, and three hours later the fatty acid was given by means of a gastric tube. The results of these tests are summarized in table 4.

The data presented in table 4 show that the saturated fatty acids, caproic and myristic, of 6 and 14 carbon numbers, respectively, increased the serum cholesterol level when administered for three days, 2 ml./day. Compared with a 243% increase for the control group receiving only cholesterol, the serum cholesterol levels went up 308 and 334%, respectively. Oleic acid with one double bond, iodine value 89.9, carbon number 18, exerted moderate anticholesterolemic activity: 182% against 243% for the controls. Undecylenic acid, one double bond, iodine value 133.0, carbon number 11, was less active than oleic acid. Thus carbon number seemed to be important for anticholesterolemic activity. When the carbon number was the same, as is the case of linoleic and linolenic acids, carbon number 18, the iodine value contributed to the activity of fatty acids. Linoleic acid with iodine value 179.5 and two double bonds was much less active than linolenic acid with iodine value 270.0 and three double bonds. Cottonseed oil was found to be only slightly active, possibly due to the presence of 27.2% saturated fatty acids. Safflower oil, iodine value 170.4, containing no saturated fatty acids, was more active than safflower oil, iodine value 143.9, containing 14% saturated fatty acids. The most active fraction was that of Pilchard (sardine) oil, iodine value 300.0, containing no saturated fatty acids, and with 82% of unsaturated fatty acids of carbon number 20, 22, and 24. There was an increase of only 47.5% in serum cholesterol concentration as compared with the initial figures before cholesterol and the fraction were administered. Almost the same activity was observed with cod liver oil, iodine value 252.0, containing no saturated fatty acids, and 82% of unsaturated fatty acids with carbon number 20 and 22. Yet this fraction gave figures lower than those of Pilchard oil, iodine value 300.0. These assays seem to indicate that both iodine value and carbon number play an important role in the serum cholesterol decreasing activity of unsaturated fatty acids.

DISCUSSION

As in the case of hypertension, which condition was believed for many years to be an attribute of aging, spontaneous hypercholesterolemia might not be necessarily a manifestation of old age. In this respect one might be inclined to agree with Sperry and Webb (34) that constitutional and dietary factors play a prime role in this condition, which is believed to contribute to atherosclerosis. The present study on young rabbits, conducted over a number of months, gives support to that postulate. The role of dietary factors, specifically of dietary fat, in causing atheromatosis, is still not resolved. In an attempt to determine the influence, if any, of iodine value and carbon number of fatty acids on experimental hypercholesterolemia, a method of three-day fasting was employed in this investigation. According to Wolff and Brignon (43), the data obtained on anticholesterolemic properties of fatty acids and oils by the fasting method correspond to the data supplied by a long-term feeding experimentation. The intrinsic relationship between fasting and serum cholesterol levels is not as yet defined. Lyon and associates

TABLE 3. EFFECT OF CHOLESTEROL FEEDING ON SERUM CHOLESTEROL LEVELS IN RABBITS.

Groups	Number of Rabbits	Average Weight (Gm.)	Average Age (Days)	Serum Cholesterol (Hours)		% Increase Cholesterol Concentration
				24	96	
I	8	1055 ± 35	49	56.1 ± 7.5	187.3 ± 6.9	233
II	8	5560 ± 90	737	60.2 ± 6.3	200.8 ± 7.4	231
III	6	5352 ± 110	721	81.1 ± 9.5	324.9 ± 9.9	300

TABLE 4. INFLUENCE OF IODINE VALUE AND CARBON NUMBER ON SERUM CHOLESTEROL LEVELS IN RABBITS.

Compound	Iodine Value	Carbon Number	Number of Rabbits	Average Weight (Gm.)	Serum Cholesterol 24	Serum Cholesterol 96	% Increase Cholesterol Concentration
Fasting only	—	—	6	1620	49.3 ± 2.5	76.4 ± 3.4	55
Cholesterol only	—	—	32	2123	70.1 ± 9.6	240.1 ± 9.9	243
Saturated Fatty Acids							
Caproic	0	6	6	1995	60.2 ± 3.2	245.2 ± 7.5	305
Myristic	0	14	6	2033	55.2 ± 2.6	239.9 ± 8.4	334
Unsaturated Fatty Acids							
Oleic, U.S.P. Saponification value 199	89.9	18	6	2246	50.1 ± 7.8	141.1 ± 9.3	182
Undecylenic Saponification value 303	133	11	6	1878	62.3 ± 8.9	186.9 ± 7.5	200
Linoleic	179.5	18	6	2305	70.4 ± 9.9	145.7 ± 10.2	107
Linolenic	270.9	18	6	1899	79.6 ± 7.7	120.0 ± 8.5	65
Vegetable Oils							
Cottonseed Saturated fatty acids 27.2% Unsaturated fatty acids 72.8% Linoleic acid 47.8% Oleic acid 22.9%	110	6 — 18	6	2008	80.2 ± 7.9	225.7 ± 9.3	206
Safflower Saturated fatty acids 14.0% Unsaturated fatty acids 86.0% Linoleic acid 78.0% Oleic acid 8.0%	143.9	6 — 18	6	1820	85.4 ± 7.8	213.5 ± 6.6	150
Safflower Saturated fatty acids 0 Unsaturated fatty acids 100% Linoleic acid 88.0% Oleic acid 12.0%	170.4	18	6	1758	66.5 ± 9.8	141.5 ± 10.2	113
Unsaturated Fatty Acid Fractions from Fish Oils							
Pilchard (sardine) Saturated fatty acids 53.0% Unsaturated fatty acids 47.0% (No fatty acids with carbon numbers 20, 22, and 24)	60.0	8 — 16	5	1880	55.0 ± 4.6	199.2 ± 9.3	262
Pilchard Saturated fatty acids 23.0% Unsaturated fatty acids 77.0% Fatty acids 48.0%	200.0	20 — 24	8	1759	60.2 ± 8.8	130.5 ± 10.2	117
Pilchard Saturated fatty acids 0 Unsaturated fatty acids 100% Fatty acids 82.0%	300.0	20 — 24	8	2232	81.4 ± 5.6	120.2 ± 8.7	47.5
Cod Liver Saturated fatty acids 15.0% Unsaturated fatty acids 85.0% Fatty acids 36.0%	167.0	20 — 22	8	1856	72.4 ± 4.4	137.4 ± 8.8	89.4
Cod Liver Saturated fatty acids 0 Unsaturated fatty acids 100% Fatty acids 82.0%	252.0	20 — 22	8	2010	85.2 ± 11.3	139.2 ± 11.2	62

(24) revealed that an 18-hour fast resulted in a 90% decrease in incorporation of labeled acetate. Catravas and Anker (4) found that the livers of the fasted rats incorporated only one-fourth as much carboxy-labeled acetate as did those from non-fasting rats. In our assays there was a moderate increase in serum cholesterol concentrations of rabbits fasting 4 days, which might indicate a slight impairment in hepatic function due to fasting. It is from this point of view that the three-day fasting procedure might be of particular interest, as revealing the property of fatty acids to decrease serum cholesterol levels under conditions unfavorable to cholesterol metabolic processes and in the absence of the factors, such as oil vehicles for cholesterol administration, which by themselves might interfere with the proper evaluation of the results of assays.

SUMMARY

Fourteen saturated and unsaturated fatty acids and unsaturated fatty acid fractions from vegetable and fish oils were tested for their anticholesterolemic properties by a three-day fasting method on rabbits.

Both the carbon number and the iodine value influence the anticholesterolemic activity of fatty acids. The fatty acid fractions of Pilchard and cod liver oils, iodine values of 300.0 and 252.0, carbon number 20-24 and 20-22, respectively, and linoleic and linolenic acids, iodine values 179.5 and 270.9, respectively, carbon number 18, showed the highest degrees of anticholesterolemic properties.

Fourteen out of 20 young rabbits, 43 days of age, observed for a period of 12 months, showed no increase in the serum cholesterol concentrations.

An opinion was expressed that spontaneous cholesterolemia might not be necessarily an attribute of aging and that constitutional and dietary factors are responsible for this condition.

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ON THE PRODUCTION OF OSTEOMALACIA BY DIETARY MEANS*

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The concept of osteomalacia is not one which is well defined, especially on an experimental basis. Possibly this is due to the difficulties which have been encountered in experimentally duplicating the clinical picture of this condition.

It is usually assumed that osteomalacia is the adult form of rickets, but a rachitogenic diet does not produce the osteoid borders of the bone trabeculae in the adult that the pathologist regards as diagnostic of osteomalacia.

Another conception of osteomalacia is that this is a condition with bone demineralization to such an extent that pain results from ordinary stresses. This might be pictured anatomically as infantile bone in the adult but with this difference physiologically: ordinary stresses on infant bone do not produce pain whereas if adult bone is demineralized to the same extent, ordinary stresses result in pain.

Our definition of osteomalacia is a decrease in the ratio of bone salts to protein matrix as compared with a normal animal of the same age. Using x-ray evidence during the past 35 years, low phosphate diets produce rickets in rats and low calcium diets produce osteoporosis. So-called low calcium rickets is a classification of the arrangement of cartilage cells in the metaphysis of the long bones and does not show up on x-ray films of rats.

Low phosphate diets that produce rickets in rats may be divided into two groups: 1) those on which the rats die in a few weeks and 2) those on which the rats recover from rickets without a change in diet, but with a slowing of the growth rate. Rats seem to develop a resistance to these diets.

With the ordinary rickets-producing diets described in the literature, osteomalacia has not been produced; therefore we have spent some years in devising more severe diets and in refining the diagnosis of osteomalacia.

In osteomalacia, the osteoid tissue is mainly collagen (ossein) of about 17.8% nitrogen but with some osseoalbuminoid of about 11.7% nitrogen. In the whole bone there is also a little protein in marrow and blood vessels. We found that rat bones, after removal of the fat, water, and mineral matter contained 15% nitrogen and so used this figure to convert the Kjeldahl nitrogen content of fat-free bone into osteoid protein ($N \times 6.667 =$ protein). These values were always checked by determining the loss in weight on incineration of fat-free dry bone.

The use of compact bone would eliminate the proteins of the bone marrow but not the osseoalbuminoid (16% N) of the Haversian canals. It is hoped that the marrow error is the same in the demineralized animals and the controls and that our figures for ossein mineralization are proportionately low in both.

Although it is very convenient to start with dry, fat free bone, fresh bone resembles the live bone more closely, and lends itself better to density analysis on x-ray films. Therefore the results of our study are tabulated in percentage of the fresh bone.

MATERIAL AND METHODS

Diet 0, listed in table 1, containing 0.228% phosphorus, only half of which was available because it was in phytin, and 0.022% calcium was judged adequate for rats in all other ingredients as it supported maximum growth of rats after the addition of 2% $Ca_3(PO_4)_2$. Diets 1-5 are given in table 2.

The 30 rats used in this study were given Philadelphia city water to drink, which contains a trace of calcium, but not appreciable in comparison with the high concentration of calcium in the diets of all rats except those on a low calcium-high phosphorus diet (rats 31 and 32, tables 2 and 7). The ears of Wistar strain rats were punched for identification and the rats placed on the diets at 21 days of age and when the body weight was about 50 Gm. Rats were weighed daily. Those on diets 1-3 grew at a slower rate than on diet 5 (fig. 1). The

* This investigation was supported in part by research grant A-602(C3) from the U. S. Public Health Service, National Institutes of Health.

We are indebted to the Endocrinology Study Section, National Institutes of Health, and to Parke, Davis & Company for Growth Hormone (STH); to Merck, Sharp & Dohme for Vitamin A, Riboflavin, Thiamine, and Pyridoxine; to the Dow Chemical Company for dl tryptophan, and to Dupont de Nemours for l lysine and dl methionine and to Standard Brands for Fleischmann's Active Dry Yeast.

TABLE 1. DIET 0.

Ingredients	Grams
Corn oil (Mazola)	100.00
Yellow corn freshly ground in a coffee mill	4143.77
Active dry yeast (Fleischmanns)	50.00
Alfalfa meal	50.00
Liver powder (Armour's)	50.00
Blood fibrin (Armour's)	500.00
Sodium chloride	100.00
Methionine	2.00
Tryptophan	2.00
Lysine	2.00
Niacin	.10
Thiamine	.01
Riboflavine	.01
Vitamin A, 50,000 units	.10
Pyridoxine	.01

fact that rats on diet 5 grew at a normal rate showed that the dietary ingredients other than mineral were normal. Since sex differences were no greater than individual variations, the sexes were not segregated in the tables.

At the end of each experiment the rats were killed with ether, weighed, and x-rayed. The left femur was dissected out, boiled 1 minute in distilled water, cleaned under magnification, and weighed immediately. It was then dehydrated with alcohol to break bond between lipoid and protein, extracted with 1 part of alcohol plus 1 part of ether in a Wiley continuous extractor for 2 days, dried in an oven at 100 C. for 2 days, weighed and ashed in a weighed porcelain boat at 550 C. for 3 hours, then weighed again, dissolved in normal HCl, and analyzed for calcium. The right femur was similarly cleaned and weighed, crushed in a diamond mortar, extracted, dried, weighed, and aliquoted for Kjeldahl nitrogen. The calculated protein was checked by the loss of weight on incineration of the left femur.

The calcium anaylses were made with a Beckman flame spectrophotometer. The wave length we used was 550 millimicrons (and for strontium 460.7). Owing to the depressing effect of phosphate, the standards were made of reagent $Ca_3(PO_4)_2$ dissolved in normal HCl. The ashed bone of the controls (diet 5) were dissolved in normal HCl and made up to 100 ml., whereas the most depleted bones were made up to 25 ml. and some intermediate up to 50 ml. The nitrogen determinations were made on 20-30 mg. samples of fat-free dry rat bone by the method of Ma and Zuazaga (3).

RESULTS

From Table 3 it may be seen that whereas rat 9 on diet 5 (control) for 100 days had a ratio of ash to protein in the femur of about 2, rats 1 to 5 on diet 1 had a ratio of about 0.5-1.4. In other words the bone matrices of the rats on diet 1 were only 0.25 to 0.7 mineralized. Some of these femurs are shown on x-ray film

TABLE 2. DIETS 1-5.

Diets	Percentage			
	Calcium	Phosphorus	Beryllium	Strontium
Diet 1 = 0 plus 3% $CaCO_3$	1.224	0.228	0	0
2 = 1 plus 1% $SrCO_3$	1.224	0.228	0	0.594
3 = 1 plus ¼% $BeCO_3 4H_2O$	1.224	0.228	0.016	0
4 = 0 plus 1% Na_2HPO_4	0.022	0.515	0	0
5 = 0 plus 2% $Ca_3(PO_4)_2$	0.795	0.628	0	0

TABLE 3. ON DIET 1 100 DAYS.

Rat No.	Body Weight at Age 121 Days	Sex	% of Fresh Femur				Ratio of Ash to Protein
			Calcium	Nitrogen	Protein	Ash	
1	158	M	6.63	4.55	30.35	16.29	.537
2	85	M	5.15	4.44	29.60	15.83	.534
3	182	M	11.47	3.56	23.77	31.62	1.333
4	208	M	11.56	3.57	23.95	31.93	1.333
5	218	M	12.52	3.54	23.58	33.73	1.430
1 mg. STH per day last 68 days							
6	167	M	9.72	3.92	26.05	28.77	1.104
7	146	F	10.33	3.95	26.37	29.21	1.108
8	152	F	11.35	4.06	26.88	30.45	1.132
Diet 5							
9	342	M	17.94	3.37	22.47	45.20	2.013

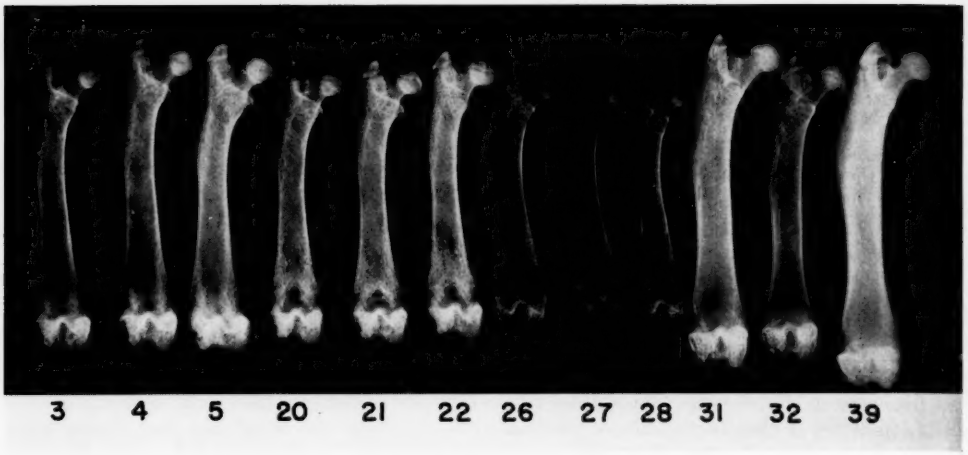

Fig. 1. X-ray of femurs of rats on various diets of different mineral content. Femurs of rats 3, 4, and 5 on diet of 1 show retarded growth and demineralization; rats 20, 21, and 22 were on diet 2 and show similar retarded growth and demineralization; rats 26, 27, and 28 were on diet 3 and show the most marked retardation of growth and demineralization (beryllium in low phosphorus diet); rats 31 and 32 were on diet 4, a low calcium diet; some degree of osteoporosis is present; and rat 39, on diet 5, a normal diet, reveals a normal femur.

TABLE 4. ON DIET 1 200 DAYS.

Rat No.	Body Weight at Age 221 Days	Sex	% of Fresh Femur Calcium	Nitrogen	Protein	Ash	Ratio of Ash to Protein
10	158	F	13.50	3.85	25.70	32.63	1.239
11	280	M	11.11	4.04	26.95	27.05	1.230
12	157	F	11.20	4.19	27.95	33.30	1.192
13	137	M	10.95	3.99	26.60	26.60	1.000
1 mg. STH per day last 86 days							
14	176	F	12.46	3.65	24.35	30.59	1.259
15	235	M	13.86	3.60	23.99	33.61	1.401
16	172	F	13.38	4.06	27.10	31.60	1.666
17	238	M	14.96	3.60	24.00	37.28	1.553
18	217	F	13.32	3.75	24.84	39.20	1.575
Diet 5							
19	400	M	16.88	3.31	22.10	45.00	2.040

TABLE 5. ON DIET 2 100 DAYS.

Rat No.	Body Weight at Age 121 Days	Sex	% of Fresh Femur Calcium	Strontium	Nitrogen	Protein	Ash	Ratio of Ash to Protein
20	145	F	9.58	0.858	3.82	25.45	27.78	1.091
21	152	F	9.74	0.928	3.59	23.94	29.80	1.245
22	168	F	9.82	0.845	3.86	25.75	29.87	1.157
23	163	F	9.32		3.88	25.9	30.6	1.182
24	165	M	8.34		3.68	24.52	27.55	1.124
Diet 5								
25	339	M	16.80		3.36	22.40	45.00	2.009

(fig. 1). Rats 6-8 which received somatotropic hormone (STH) injections the last 68 days show no difference in bone mineralization from rats 1-5, which did not receive STH.

Table 4 indicates that rats 10-18 may have partly recovered from demineralization in 200 days when compared to table 1 (100 days). Whereas the femur matrices of rats 1-8 were about 25 to 70% mineralized those of rats 10-18 were about 50 to 83% mineralized. Again STH injections 1 mg. per day for the last 86 days to rats 14-18 seemed not to have any effect on bone mineralization on diet 1.

Table 5 compared to table 1 shows that adding 1% strontium carbonate to diet 1 had little effect on bone mineralization, except that the calcium content of the bones was usually less, about 8% of the calcium being replaced by strontium. This is made evident if the calcium content of the bone ash is calculated which is about 36.9% in rat 5 and 32.9% in rat 22, the rats with the highest calcium contents on diets 1 and 2.

It may be seen from table 6 that adding 0.25% beryllium carbonate to diet 1 markedly reduced the mineralization of the femurs of rats 26-29 (the femurs being only about 30% mineralized). It also markedly reduced the calcium content of the femurs (fig. 1).

The low phosphate diets stopped the growth of the bones in length. This effect was evident in the histological appearance of the ends of the tibia, as also observed by Sager and Spargo (4). This is shown in table 7, which gives the length of the femur from the head of the femur to the median condyle, as compared with the control (rat 9, fig. 1). The animals crouched and squealed when handled, as if these manipulations were painful.

It may be seen from table 7 that low phosphate diets 1-3 retarded the growth in length of the femur more than low calcium diet 4. This seems to be contrary to past experience with low calcium diets. This seeming contradiction is explained by the fact that it is more difficult to prepare a diet, adequate in other ingredients, but low in phosphate, than it is to prepare one low in calcium; and many diets prepared in the past were not low enough in phosphate to stop growth. Strontium (rats 20-22) further reduced the growth in length, and beryllium (rats 26-28) was more effective than strontium (fig. 1 and table 7).

The rats on high calcium diets had kidney and bladder stones as also pointed out by Sager and Spargo (4). Some of the bladder stones were detectible in x-ray plates, but none of the kidney stones could be detected by x-ray (fig. 2). These stones were found at autopsy.

DISCUSSION

Since Wistar strain rats become sexually mature at 50-60 days, our rats at 121-122 days should be considered adult, and therefore we are not dealing with rickets, although the rats showed beading of the ribs and bone demineralization accompanied by pain.

The rat has a remarkable power of adaptation to changes in the calcium and phosphorus of the diet, which may be carried over from mother to offspring. But after becoming adapted to one level it may take the rat a long time to become adapted to an entirely different level. In figure 3 the lowest curve shows the growth rate of a male rat adapted in utero and during the first 21 days to diet 4, very low in calcium and then placed on diet 1, very high

Fig. 2. Rat No. 4 on a high calcium low phosphorus diet developed a stone in the bladder.

TABLE 6. RATS ON DIET 3 100 DAYS.

Rat No.	Body Weight at Age 121 Days	Sex	% of Fresh Femur				Ratio of Ash to Protein
			Calcium	Nitrogen	Protein	Ash	
26	164	M	6.00	3.94	26.25	16.25	.619
27	122	M	4.05	4.26	28.4	13.2	.464
28	124	F	6.02	3.81	25.57	16.42	.642
29	115	F	4.12	4.05	27	16.05	.590
Diet 5							
30	350	M	16.70	3.39	22.60	45.30	2.005

TABLE 7. LENGTH OF FEMUR OF RATS ON VARIOUS DIETS.

Rat No.	Length of the Femur in Millimeters at Age 121 Days	
3	31.25	
4	32.30	Diet 1, high calcium, low phosphate
5	31.80	
20	29.75	
21	29.70	Diet 2, high calcium and strontium, low phosphate
22	30.25	
26	28.50	
27	27.00	Diet 3, high calcium and beryllium, low phosphate
28	26.50	
31	35.00	Diet 4, low calcium, high phosphate diet
32	32.25	
9	36.50	
25	36.0	Diet 5, normal control
30	34.5	

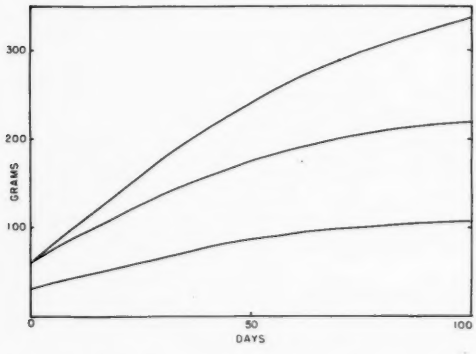

Fig. 3. Growth curves of male rats. The upper curve is of a male rat on diet 5 whose mother was fed diet 5, a normal diet. The middle curve is of a rat on diet 1 whose mother was fed diet 5. The lower curve is of a rat on diet 1 (high in calcium and low in phosphate) and whose mother was on diet 4 (low in calcium and high in phosphate).

in calcium. This curve may be compared to the middle curve of a rat not adapted to diet 4 before being placed on diet 1.

Perhaps the mechanisms of the adaptation to the low phosphate diet are the cessation of activity of the parathryoid glands and the cessation of the growth of the long bones in length. This is why we tried to determine the effect of STH, the daily injection of which at doses of 1 mg. per rat per day had no effect.

The phosphate content of 0.228% of the diets may not seem very low, but about half of the phosphate was in phytin and so unavailable. The addition of 3% $CaCO_3$ to the diets made more of the phosphate unavailable by precipitation in the intestine. If more than 3% $CaCO_3$ is added to the diet, the rats become unthrifty, but whether this was due to increase in kidney and bladder stones was not determined. The action of strontium is probably in precipitation of more phosphate in the intestine. Beryllium is said to act in the same way or at least to lower the inorganic phosphate of the blood plasma (1). We are not merely producing beryllium rickets, as the percentage of beryllium in the diet was too low to produce rickets on a diet of normal phosphate content. Beryllium also inhibits the action of alkaline phosphatase (2).

SUMMARY

We have found that low phosphate diets deficient in vitamin D when fed for 100-200 days produce osteomalacia in the rat. Perhaps the reason this has not been done before is because rats on low phosphorus diets are hard to maintain into adult life. We have spent several years testing diets that would produce osteomalacia on low phosphorus diets without resulting in early death of the animal. Instead of using the microscope to determine the amount of decalci-

fication, we resorted to chemical analysis, using the ratio of ash to protein. In the normal rat this ratio was 2, but in osteomalacia it was 0.5 to 1.5. Our previous studies have shown that in osteoporosis, this ratio was normal.

In osteomalacia, growth activity was retarded at the ends of the long bones.

Rats developed various degrees of adaptation to these diets.

Additions of strontium or beryllium, too small to produce effects by themselves, intensified the effects of the very low P/Ca ratio.

Bladder stones were observed by x-ray and autopsy, and kidney stones were found at autopsy in rats fed high calcium diets.

Animals with osteomalacia exhibited painful reactions when handled, whereas these reactions were not present in animals with osteoporosis.

These experimental findings serve to more clearly differentiate osteomalacia from osteoporosis and help to clarify the dietary factors which are involved.

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HISTOCHEMICAL LOCALIZATION OF ENZYMES DEPHOSPHORYLATING ATP AND AMP IN ANIMAL AORTAE

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MATERIAL AND METHODS

The present study was undertaken with the purpose of investigating by histochemical methods the distribution of enzymes dephosphorylating ATP and AMP in the aorta of 8 cats and 15 rats. All specimens were alcohol and acetone-fixed, and wax-embedded.

The technique used was similar to that described by Gomori (2), with the exception that ATP replaced sodium glycerophosphate in one series of sections of the aorta and AMP in a second series. In addition a third series was treated by the standard Gomori alkaline phosphatase technique (pH 9.0) in order to distinguish the results we obtained from those due to non-specific alkaline phosphatase. Optimum pH when either ATP or AMP were used was found to be 8.4. Incubation times of 4, 8, 12, and 24 hours were used for all three series. All the animals were under middle age.

RESULTS AND DISCUSSION

The standard non-specific phosphatase reaction was negative in the intima and media and all parts of all the aortae. The adventitia was positive with all substrates at all levels. When cross sections of the aortae of the cat and rat were studied using ATP and AMP as substrates, some sections were found to be completely negative and others strongly positive, although the conditions of fixation and incubation were identical. It was thought that this might be due to a regional difference in the aortae. Longitudinal sections of complete aortae were therefore incubated with AMP as substrate, and it was found that a strong regional localization of enzyme activity of the aorta existed and that the activity was intense in the aortic arch and descending thoracic aorta and completely negative in the abdominal aorta (fig. 1-5). Further reference to the cross sections in which both AMP-ase (5-nucleotidase) and (heat stable) ATP-ase activity had been previously demonstrated showed in fact that all the negative sections had been from the abdominal regions and all the positive from the arch or thoracic aorta.

Detailed observations on the longitudinal sections of the aortae demonstrated that the heart muscle at the site of origin of the aorta was virtually negative as described by Beckett and Bourne (1); the aorta at its origin was negative and the ascending limb became increasingly positive as the arch was approached. Most intense activity was in the arch and descending thoracic aorta. The descending aorta decreased in activity as it approached the level of the diaphragm and by the level of the coeliac vessels it was completely negative.

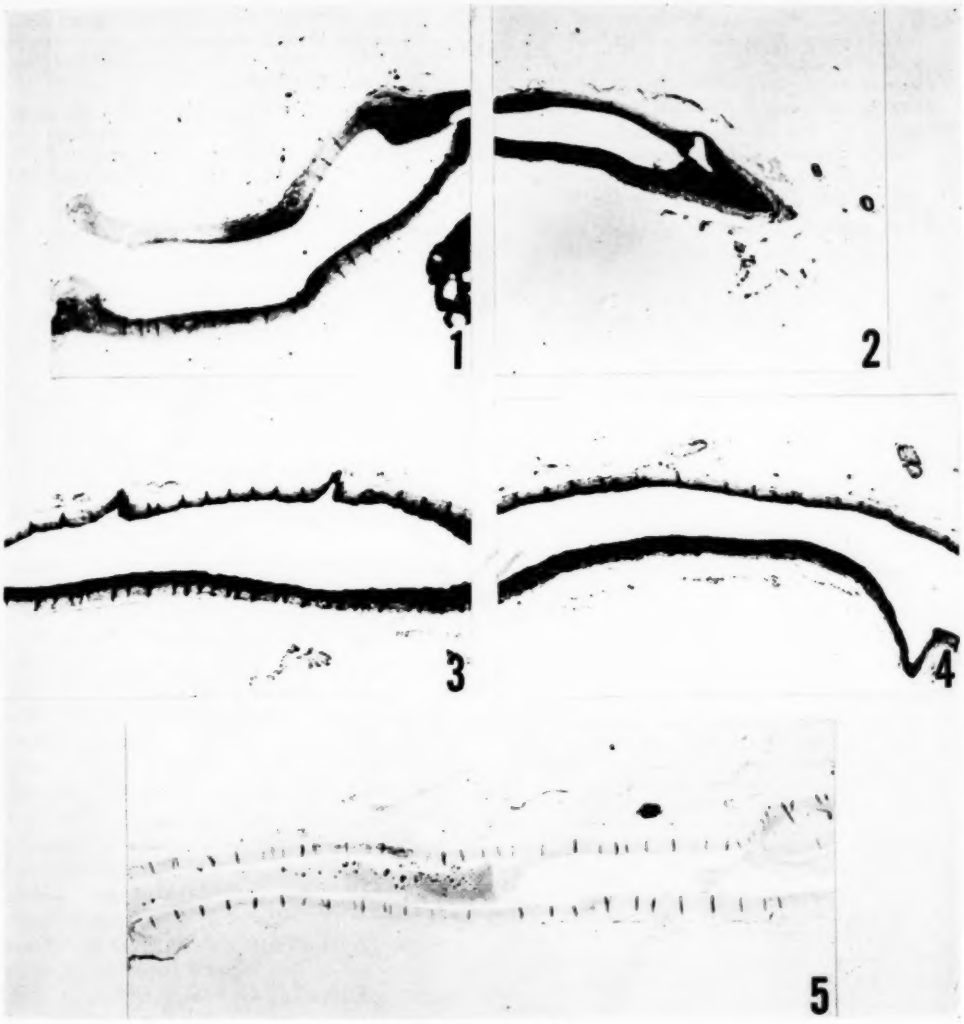
Popják (5) has shown in experiments with liver homogenates *in vitro* that ATP is necessary for the synthesis of cholesterol and that it needs to be added continuously or in large quantities to the incubating medium. This was thought to be due to the fact that dephosphorylating enzymes present in the liver actively hydrolyze phosphate esters and that this is possibly the method whereby the production of cholesterol and lipids is limited in the thoracic aorta. Our finding that there is a lack of adenosine dephosphorylating enzymes in the abdominal aorta might explain why there is an increased intensity of atherosclerotic lesions in this part of the vessel.

It is of interest in this connection that Kirk (4) has shown that the mean adenylpyrophosphatase and inorganic pyrophosphatase activities of the arteriosclerotic aortic and coronary artery tissues were moderately lower than the activities of the normal tissue of the same arteries.

It is important to note that in a previous work Kirk (3) has studied only the thoracic part of the aorta, and since in this paper he does not specify which part was used, we assume that he refers again only to the thoracic part.

Furthermore it should be noted that Werthessen (6) has shown in perfusion experiments

This work was carried out under a grant from the Georgia Heart Association and with equipment provided by the Emory University Research Committee.



5-Nucleotidase in Cat Aorta

Fig. 1. Ascending aorta and portion of arch. Origin from heart to the left. Increasing activity is shown from origin to arch.

Fig. 2. Descending portion of aortic arch. Intense positive reaction.

Figs. 3. & 4. Thoracic aorta. Intermediate activity.

Fig. 5. Abdominal aorta below coeliac region. Reaction completely negative.

on the cow's aorta that there is a greater production of lipid material in the abdominal part of the aorta as compared with the thoracic part.

SUMMARY

A study of 8 cats and 15 rats shows a gradient of activity for the 5-nucleotidase and heat-stable ATP-ase. These enzymes are most active in the arch and thoracic part of the aorta and lacking in activity in the abdominal part.

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THE TOTAL GLUTATHIONE CONTENT OF ARTERIAL TISSUE IN INDIVIDUALS OF VARIOUS AGES*

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Although the glutathione content of several tissues has been established, no investigations of the glutathione concentration of human arterial tissue have as yet been reported. The present study was undertaken with the purpose of supplying such data. The procedure of Dohan and Woodward (2) was employed for electrolytic reduction of the oxidized glutathione; the total reduced glutathione was subsequently determined by amperometric titration.

MATERIALS AND METHODS

Sixty-three samples of the thoracic descending aorta and 24 samples of the pulmonary artery were included in the study; the samples were obtained fresh at autopsy at the St. Louis City Morgue. After removal of the adventitia the samples were rinsed briefly with cold isotonic sodium chloride solution to eliminate contamination from adhering blood. Ten % homogenates of the intima-media layers of the samples were prepared with 4.0% sulfosalicylic acid; the homogenates were subsequently centrifuged for 10 min. at 4000 r.p.m. and the supernatants used for the glutathione determinations. In the case of the aortic samples the glutathione measurements were performed separately on normal and arteriosclerotic sections of the same blood vessels.

The electrolytic reduction of the oxidized glutathione was carried out essentially as described by Dohan and Woodward (2). For the cathode compartment a 30 ml. beaker with a diameter of 3.2 cm. was used; enough mercury was added to the beaker to provide an 8 to 10 mm. mercury layer. Three ml. of the arterial homogenate supernatant, corresponding to 300 mg. of wet tissue, were transferred to the cathode compartment, after which 1.0 ml. of 4.0% sulfosalicylic acid and 1.0 ml. of water were added to the sample. The anode compartment contained 10.0 ml. of 4.0% sulfosalicylic acid. The two compartments were connected by means of a KCl-agar salt bridge. For the electrolytic reduction a direct current of 34 milliamperes was used, yielding a current density of 4.2 milliamperes/cm.^{2} The reduction time employed was 20 min., during which period the sample was stirred continuously by means of a mechanical stirrer placed immediately above the surface of the mercury.

For iodometric titration of the quantity of reduced glutathione present in the sample, a 2.0 ml. aliquot of the electrolytically reduced solution was pipetted into a 50 ml. beaker (cathode compartment). To the aliquot was added 0.5 ml. of a solution containing 5.0% of potassium iodide and 0.5% of hydroxylamine; this was followed by addition of a sufficient quantity of 2.0% sulfosalicylic acid to make a final volume of 10.0 ml. The anode compartment contained 9.5 ml. of 2.0% sulfosalicylic acid, 0.5 ml. of 5.0 potassium iodide solution, and 3 drops of a 0.1 N solution of sodium thiosulfate; this latter reagent served to keep the anode depolarized. The two compartments were connected by means of a KCl-agar salt bridge. The amperometric titration was performed with a 0.0001 N solution of KIO_3 using a Sargent Manual Polarograph Model III; the potassium iodate solution was prepared fresh before use by dilution of a 0.005 N stock solution. The average error between duplicate determinations was 2.9%.

Since ascorbic acid is also included in the iodometric titration the glutathione content of the sample was obtained by correcting the total titration value for the small amount of ascorbic acid present in the sample, this latter value being determined on another aliquot of the supernatant through visual titration with 2,6-dichlorophenolindophenol (1).

Oxidized glutathione was recovered quantitatively as reduced glutathione following the electrolytic reduction both in analyses of a standard solution of the compound and following addition of the oxidized glutathione to samples of arterial homogenates.

It has been shown by Dohan and Woodward (2) that the electrolytic procedure does not cause reduction of dehydroascorbic acid; this observation was confirmed in experiments on a solution of this compound prepared from a sample obtained from K & K Laboratories, New York.

RESULTS

The mean concentrations of total glutathione found in aortic and pulmonary artery samples for various age groups have been listed in table 1.

Aortic samples.—The average glutathione value observed for the 63 normal aortic samples was 0.22 mg./Gm. wet tissue. As seen from the standard deviations listed in table 1 the variation in the tissue content of glutathione was rather high. A tendency was noted for the glutathione concentration of the aortic tissue to

* Studies on Arterial Metabolism XXVIII. The investigation was supported by a grant from the National Institutes of Health, Public Health Service (PHS-891).

TABLE 1. MEAN GLUTATHIONE CONCENTRATIONS OF HUMAN ARTERIAL TISSUE IN VARIOUS AGE GROUPS.

Age Group (Years)	N	Cholesterol, % of Wet Weight	Mg. Glutathione/Gm. Wet Tissue	s.d. of distr.	Mg. Glutathione/Gm. Tissue N	s.d. of distr.
Normal Aortic Tissue						
0-19	11	0.17	0.19	0.11	4.2	2.4
20-49	26	0.36	0.19	0.13	4.6	3.6
50-59	11	0.43	0.22	0.09	5.8	2.5
60-79	15	0.50	0.29	0.12	8.9	4.0
Grand Mean			0.22	0.13	5.6	3.7
Arteriosclerotic Aortic Tissue						
20-49	11	1.00	0.22	0.12	7.5	5.6
50-59	9	1.14	0.19	0.16	6.0	5.6
60-79	10	1.03	0.28	0.10	8.7	4.0
Grand Mean			0.23	0.13	7.5	5.0
Pulmonary Artery Tissue						
0-19	2	0.10	0.37	—	9.8	—
20-49	8	0.21	0.23	0.12	6.8	3.9
50-59	5	0.31	0.25	0.07	7.5	2.2
60-79	9	0.26	0.30	0.14	9.8	4.2
Grand Mean			0.27	0.12	8.3	3.7

increase with age; the coefficient of correlation between age and tissue glutathione content was + 0.27 (t = 2.18, N = 63) when calculated on the basis of wet tissue weight, and + 0.40 (t = 3.24, N = 63) when expressed on the basis of tissue nitrogen content.

In view of the rather high variation observed for the glutathione concentrations, the values were subjected to further analysis. The average value found for 19 samples from female individuals (mean age, 40 years) was 0.20 mg./Gm. wet tissue, and the corresponding value for 44 samples from male subjects (mean age, 44 years) was 0.23 mg./Gm. wet tissue. No significant difference was found either between the glutathione content of 38 samples from white subjects (mean age, 46 years) and 25 samples from colored individuals (mean age, 37 years), the average values being, respectively, 0.23 and 0.21 mg./Gm. wet tissue.

Twenty of the aortic samples were obtained from persons who had died as the result of a traumatic accident. The mean glutathione concentration observed for these samples was slightly lower (0.17 mg./Gm. wet tissue) than the average value of 0.24 mg./Gm. wet tissue recorded for the remaining 43 samples. This difference may be due to the fact that the mean age of the individuals who had suffered accidental death was only 34 years. A higher mean glutathione value of 0.27 mg./Gm. wet tissue was found for 14 subjects who had died from cardiac disease; the average age of the persons in this group was 56 years.

A comparison was made of the glutathione content of arteriosclerotic and normal tissue portions of 30 aortic samples. In 10 of the 30 samples the difference was less than 0.05 mg./Gm. wet tissue; in 7 cases the glutathione concentration of the arteriosclerotic tissue was 0.10 to 0.22 mg./Gm. lower, and in another 7 cases 0.10 to 0.34 mg./Gm. higher than the values observed for the normal tissue of the same blood vessels. The average glutathione content of the arteriosclerotic tissue was 97% of the mean value of the normal tissue, when expresed on the basis of wet tissue weight (t of diff. = 0.39, N = 30) and 101% when calculated on the basis of the tissue nitrogen content (t of diff. = 0.12, N = 30).

Pulmonary artery samples.—The mean glutathione value observed for the 24 pulmonary artery samples (0.27 mg./Gm. wet tissue) was moderately higher than the average value found for the normal aortic samples. A comparison of the pulmonary artery glutathione values with those of the normal aortic samples from the same subjects failed, however, to reveal any significant difference, the t-value of the difference being 1.06 (N = 24) when expressed on the basis of wet tissue weight, and 1.93 when calculated on the basis of the tissue nitrogen content. The coefficients of correlation between age and pulmonary artery glutathione content were + 0.21 (t = 1.02, wet tissue weight) and + 0.12 (t = 0.52, tissue nitrogen content).

SUMMARY

Determinations were made of the total glutathione concentration of 63 samples of the thoracic descending aorta and 24 samples of the pulmonary artery obtained fresh at autopsy from individuals of various ages. The procedure of Dohan and Woodward was used for electrolytic reduction of the oxidized glutathione; the total reduced glutathione was determined by amperometric titration. In the case of the aortic samples the glutathione determinations were made separately on normal and arteriosclerotic portions of the same blood vessels.

The average glutathione values observed for the normal aortic, arteriosclerotic aortic, and pulmonary artery samples were, respectively, 0.22, 0.23, and 0.27 mg./Gm. wet tissue. A tendency was noted for the glutathione concentration of the normal aortic tissue to increase with age, the coefficient of correlation between age and tissue glutathione content being + 0.27 ($t = 2.18$) when calculated on the basis of wet tissue weight, and + 0.40 ($t = 3.24$) when expressed on the basis of the tissue nitrogen content.

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THE FREE RADICAL THEORY OF AGING: THE EFFECT OF AGE ON SERUM MERCAPTAN LEVELS

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Aging has been postulated to be in part the result of the side effects of free radicals (for example, HO and HO_2) normally produced in the course of metabolism or by the interaction of O_2 with oxidation catalysts (such as iron, copper, and cobalt) in the intracellular spaces (2). It would be expected that the free radicals would exert their effects, for the most part, by initiating oxidation reactions.

The rate of aging, as measured by the log of the mortality rate, is proportional to age. Hence, in terms of the free radical aging theory, it would be predicted that the rate of oxidation at any given time depends on the age, or in other words, the over-all extent of oxidation of the body, i.e., $\frac{dO_2}{dt} = kO_2$, where O_2 stands for the extent of oxidation. Since it is the more easily oxidized compounds of the body that would be expected to be involved primarily in these free radical reactions, their concentration might decrease with age; this paper reports the effect of age on serum mercaptan levels.

MATERIAL AND METHODS

Fasting blood was collected by venepuncture, using vacuum tubes, from 35 normal university personnel in the age range of 20 to about 60 years, while blood from 9 individuals above age 60 was obtained for the most part from patients seen in a medical clinic for minor ailments.† Generally 4 to 5 samples of blood were processed per day. The blood was allowed to clot, and after 20 to 60 min. (although serum mercaptan values were found to decrease with time of standing, it was not significant for periods less than one hour) the tubes were centrifuged for 10 min. using an International Clinical centrifuge at 3000 r.p.m. The clear serum (no hemolysis) was decanted off and recentrifuged for 5 min., as occasionally a few red cells came over from the sediment. Following this, 2 ml. of the clear, fresh serum were stirred into 58 ml. of aqueous methanol (400 ml. of methyl alcohol diluted to 1000 ml. with distilled water). Two ml. of a supporting electrolyte (30 Gm. of NH_4NO_3 were added to a 250 ml. volumetric flask containing 125 ml. of concentrated NH_4OH and 100 ml. water; the resulting solution was brought to room temperature and made up to 250 ml. with distilled water) were then added and the mercaptan groups of the clear solution titrated with 0.00091 M $AgNO_3$; the end point was determined by measuring the current flowing between a mercury-mercuric iodide electrode and a rotating platinum electrode with a sensitive galvanometer (5) as a function of the amount of $AgNO_3$ added, the end point being taken as the intersection of the extension of the two straight portions of the curve. No change was noted in the accuracy of the method over the period of study as evidenced by the constancy of the values obtained for a dilute solution of dodecyl mercaptan in methyl alcohol; the 9 determinations made over the period of this study (5 months) ranged from 1.20 to 1.28 ml. of the $AgNO_3$ solution with a mean value of 1.24 ml. Rechecks on serums were within 5%. Blood samples obtained in different weeks from 4 individuals indicated that fasting serum mercaptan levels may be fairly constant in a given person (table 1).

RESULTS

The data, expressed as milliliters of 0.00091 M $AgNO_3$ per 2 ml. of serum for men and women are presented in figures 1 and 2, respectively; these data can be converted to μM SH/100 ml. of serum by multiplying by 45.5.

As seen from figure 1, the serum concentration of mercaptan groups of normal males decreased with age from a level of about 55 μM/100 ml. of serum at age 20-40 to a level of about 40 μM/100 ml. of serum at age 80. The regression equation of serum mercaptan level, expressed as milliliters of 0.00091 M $AgNO_3$ per 2 ml. of serum, on age is $y = 5.59 \cdot 10^{-3} x + 1.4$, where y is ml. of $AgNO_3$ solution

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† We would like to express our appreciation to Dr. H. I. Harvey and the Medical Clinic of the Herrick Memorial Hospital of Berkeley, California, for their assistance and cooperation in this project.

TABLE 1. COMPARISON OF SERUM MERCAPTAN LEVELS OBTAINED IN THE SAME INDIVIDUALS ON VARIOUS DAYS.

Subject	μM SH/100 ml. Serum
1	67, 63
2	68, 71
3	66, 52
4	52, 54

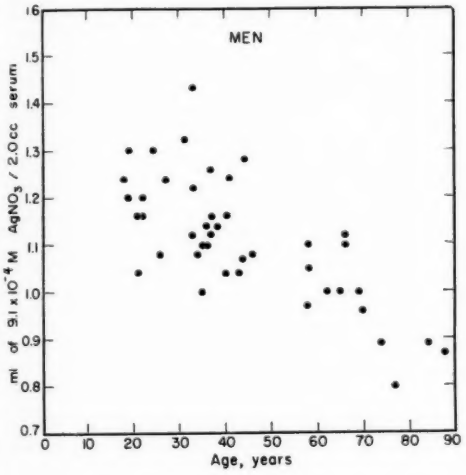

Fig. 1. Effect of age on serum mercaptan levels: Males.

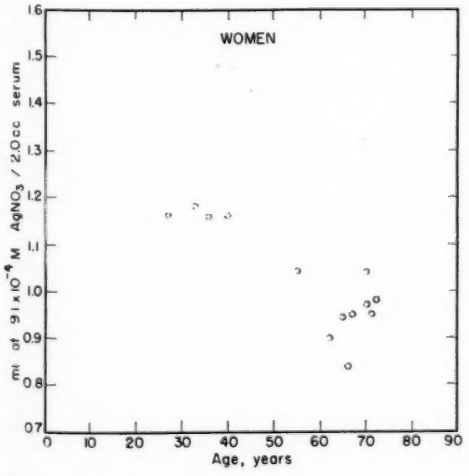

Fig. 2. Effect of age on serum mercaptan levels: Females.

and x is age in years. The correlation coefficient is 0.71 $\pm$ 0.07, significant at the $P<0.01$ level. The data for women (fig. 2) are of the same magnitude and show the same trend; however, the numbers are too few to establish the statistical validity of the relationship of serum mercaptan levels to age in women. Values for the younger individuals reported by Weissman and associates (5) agree with the average of the 20-40 group values obtained in the present study.

DISCUSSION

The decrease in mercaptan levels with age is not necessarily due to an increased rate of oxidation as postulated by the free radical aging theory. Serum mercaptan groups are attached mainly to protein (SH albumin: SH globulin = about 4:1) and to a minor extent to more readily diffusable substances such as cysteine and glutathione (5). There is apparently no marked variation in the composition or amounts of the serum protein with age (4). The possibility exists that the newly formed serum protein contains fewer mercaptan groups as the individual ages and that this accounts for the observed decrease of mercaptan levels with age rather than to an increased rate of oxidation of the serum mercaptan groups. However, supporting this latter possibility is the fact that in males ascorbic acid, which like mercaptans is easily oxidized, also decreases with age (3). In any case, the fact that the concentration of mercaptan groups in serum decreases with increasing age indicates, with other factors remaining constant, that free radical oxidation reactions may occur in the serum of elderly patients at a greater rate than in young patients.

The wide variation among people of serum mercaptan levels may be of clinical significance. On the basis of the free radical aging theory this variation may be a reflection of the variability in over-all oxidation rates in people and hence in rates of aging. Thus, people with higher serum mercaptan levels might be expected to live longer than those with lower values. In agreement with this suggestion are the results of a recent study which indicate that older persons with low blood levels of vitamin A, niacin, and ascorbic acid (all three are easily oxidized compounds) suffer a higher mortality rate than do persons with greater amounts of these substances in the blood (1).

SUMMARY

The serum concentration of mercaptan groups of 44 normal males decreased with age from a level of about 55 μM/100 ml. of serum at age 20-40 to a level of approximately 40 μM/100 ml. serum at age 80. The few data available for women were of the same magnitude and showed the same trend.

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VITAMIN B_6 DEFICIENCY IN THE AGED

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Numerous studies (1, 3, 4, 7) have been conducted to determine whether the vitamin concentration in serum decreases with advancing age. Of the various water soluble vitamins studied, an agewise regression has been demonstrated only for vitamin B_{12} (1, 3, 4) and ascorbic acid (7). The decrease in serum level of vitamin B_{12} may be attributable in part to impairment of absorption as a result of an inadequate secretion of intrinsic factor by the stomach of old individuals (5). No such associated factor is known to be involved in the absorption of ascorbic acid. Recent interest in the physiological functions of vitamin B_6 prompted us to examine whether vitamin B_6 deficiency might be common among old subjects. As indices of vitamin B_6 nutrition, we determined serum transaminase (SGOT) (9, 13, 14) and xanthurenic acid excretion after a tryptophane load test (8, 10, 11, 12). Comparisons were made between values obtained for young and old individuals. The effects of subsequent administration of pyridoxine on these phenomena also were observed.

METHOD

Selection of subjects.—Young subjects: Sera of healthy young individuals (average age, 25 years) were obtained by taking fasting specimens from the following groups of healthy subjects: (a) students and employees of the School of Hygiene, (b) physicians and interns of the Johns Hopkins Hospital, and (c) volunteers from the state penal institution. The diets were not controlled by us and probably differed considerably. The intake of vitamins and other nutrients was unknown to us.

Old subjects: Sera of healthy old individuals were obtained from three homes for the aged located in three cities, Baltimore, New York, and Philadelphia. The dietary intake of vitamin B_6 and other vitamins probably also varied considerably among these persons. The average age was 76 years.

Tryptophane load test.—In this test, 15 Gm. of dl-tryptophane mixed with orange juice or water was fed to test subjects and the 24-hour urinary excretion of xanthurenic acid, before and after the administration of the amino acid, was determined with the method of Rosen, Lowy, and Sprince (12).

Serum glutamic oxalacetic acid transaminase test.—The transaminase content in sera was measured by the method of Steinberg, Baldwin, and Ostrow (6). In our experience, when several aliquots of the same sera from the young or old subjects were analyzed, under blind code numbers, the results seldom varied more than 5% from the mean values.

RESULTS

Determination of SGOT levels in sera of young and old subjects.—The SGOT content in sera of 60 young and 62 old healthy individuals (male and female) was measured. The results (table 1) demonstrate that the SGOT content was lower in the sera of old individuals than in those of the young, regardless of the home in which the subjects were residents. A significant difference ($p < 0.05$) was obtained between any one of the three young groups (a, b, or c) and the old groups (I, II, or III). However, there are no differences among the young and old groups, regardless of the residency. No sex difference in the levels of SGOT in serum was observed (fig. 1). The SGOT serum levels of the 122 subjects are plotted against age in figure 1. An agewise regression with a slope of 0.8 unit per decade was found. In spite of the statistical significance of the regression, with the procedure of least squares and with a $p < 0.05$, it should be pointed out that the number of points falling between the ages of 35 and 70 years is small, and, therefore, the regression must be considered as tentative until more data are available.

To study the daily variations of the transaminase levels, 4 old male subjects (65 years or older) and 4 young male volunteers were chosen. They were bled every other day for two weeks for the determination of the enzymic activity. The results are tabulated in table 2.

The effect of vitamin B_6 treatment on SGOT levels of old people.—To determine whether

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the difference in the SGOT content was due to vitamin B_6 deficiency, 14 old individuals from Home I and 6 from Home II were treated daily with 15 mg. vitamin B_6 for 3 weeks and the SGOT levels were measured before and after treatment. It can be seen from the bar-graph (fig. 2) that Vitamin B_6 administration brought about an increase in the average SGOT level from 13.7 ± 1.05 to 18.7 ± 0.94 (Home I) and from 14.1 ± 0.77 to 20.5 ± 1.99 units per ml. (Home II). The response of these two groups to vitamin B_6 administration, therefore, was statistically significant in both instances, $p < 0.05$.

The effect of addition of pyridoxal phosphate to sera on SGOT activity.—To determine whether the low SGOT content was due primarily to an insufficiency of pyridoxal phosphate, the coenzyme of transaminase, pyridoxal phosphate was added, *in vitro*, to the sera of young and old subjects. The transaminase activity of the mixture was then determined. In all experiments 250 micrograms of pyridoxal phosphate was added to 0.20 ml. of the test serum to insure an adequate supply of this coenzyme. The results tabulated in figure 3 represent the effect of the addition of pyridoxal phosphate to samples of sera of 22 old and 20 young subjects. They demonstrate clearly that the *in vitro* addition of pyridoxal phosphate raised the transaminase activity of the sera of both young and old individuals from 16.1 ± 0.97 to 22.5 ± 1.8 and from 8.7 ± 0.75 to 22.0 ± 1.7, respectively. However, the increase was greater when the addition was made to sera of old subjects and was such as to bring the total SGOT activity to about equal levels in the two groups.

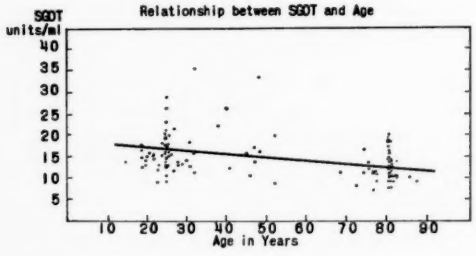

Fig. 1. Relationship between SGOT and age.

TABLE 1. SGOT CONTENT* IN SERA OF YOUNG AND OLD SUBJECTS.

A. According to Institutions

Residents of	Mean Age (yrs.)	SGOT Content Units
a) A Student Dormitory	26 (10)†	17.9 ± 0.76
b) Physicians' Dormitory	32 (8)	18.8 ± 1.60
c) A Penal Institution	23 (42)	16.5 ± 0.53
I) Home I (Baltimore)	75 (8)	12.6 ± 1.02
II) Home II (New York)	76 (39)	13.17 ± 0.49
III) Home III (Philadelphia)	74 (15)	13.37 ± 0.99

B. Composite Results

Sex	Young	Old
Male	16.5 ± 0.53	13.0 ± 0.72
Female	18.8 ± 1.58	13.3 ± 0.59

* SGOT transaminase activity is expressed as units/ml. serum.
† Number in parenthesis indicates the number of subjects used.

TABLE 2. DAILY VARIATION OF TRANSAMINASE ACTIVITY (Units/ml.).

Subjects	Age*	Period† 1	2	3	4	5	6	7
A	22	19.2	19.8	19.0	—	18.4	19.0	18.2
B	24	16.8	17.4	—	16.8	18.4	17.2	17.8
C	30	21.6	18.7	—	19.2	18.9	19.0	18.0
D	26	18.4	20.6	—	—	19.2	18.2	19.5
E	67	12.6	11.4	12.0	11.1	12.3	11.9	11.8
F	72	14.6	14.2	12.0	—	12.7	13.4	13.5
G	80	11.0	11.0	14.0	—	—	11.7	12.8
H	65	9.7	11.2	11.4	—	13.0	12.0	9.8

* Age shown in years.
† Period is of two days each.

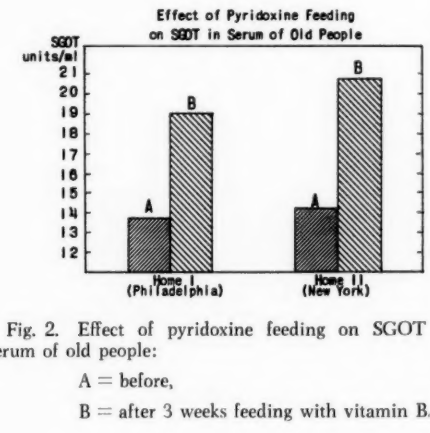

Fig. 2. Effect of pyridoxine feeding on SGOT in serum of old people:

A = before,

B = after 3 weeks feeding with vitamin B_6.

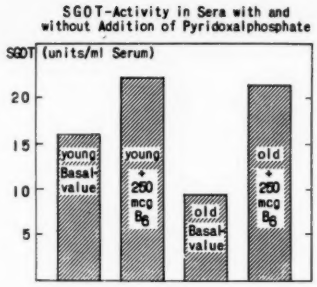

Fig. 3. SGOT-Activity in sera with and without addition of pyridoxalphosphate.

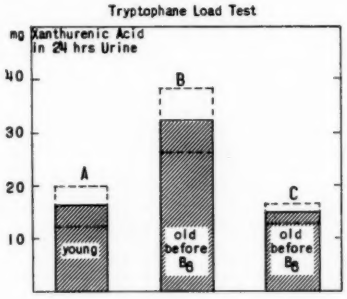

Fig. 4. Tryptophane load test:
A = in young people,
B = in old people before B_6-feeding,
C = in old people after B_6-feeding.

The excretion of xanthurenic acid after a tryptophane load.—Another test for vitamin B_6 deficiency has been developed from the observation that deficient animals are less capable of completing the normal processes of tryptophane (8, 10) metabolism and demonstrate an accumulation of xanthurenic acid after a load dose of tryptophane. The test was applied to 20 young and 24 old people and the 24-hour xanthurenic acid excretions were determined. Data in figure 4 demonstrate that the excretion of the old was about twice that of the young, 32.6 ± 6.3 and 16.5 ± 3.6 mg, respectively. However, the daily administration of 15 mg. vitamin B_6 to the old subjects for 3 weeks promptly corrected the abnormal excretion of xanthurenic acid by the reduction of excretion from 32.6 ± 6.3 to 15.4 ± 1.9 mg. in 24-hour urine specimen.

DISCUSSION

In this report we have demonstrated that there seems to be a decrease in the SGOT content with advancing age and diminution of the ability to catabolize a large amount of tryptophane. Both tests are indications of vitamin B_6 deficiency. That these findings may be due to differences in the intake of vitamin B_6 in the daily diets of young and old individuals, or differences in caloric intake has not been ruled out; however, our specimens were drawn from young and old subjects on a variety of diets and it is not likely that the observed differences in serum SGOT can be explained on the basis of differences in dietary vitamin B_6 intake alone. The role of diet could be settled, if we could obtain specimens for analysis from young and old subjects with the same dietary history and environment. These data do suggest that the agewise difference in the SGOT content is not due primarily to a progressive decrease of dietary content of vitamin B_6. On the other hand, if the intake is sufficiently large, the SGOT levels can be raised, either *in vivo* or *in vitro* with concomitant restoration of the metabolism of the essential amino acid, tryptophane. Our procedure for the determination of SGOT *in vitro* demonstrates that the protein moiety or the apoenzyme of the SGOT molecule is not diminished among the aged. The decrease in the SGOT activity is due primarily to the decrease in the coenzyme; namely, pyridoxal phosphate. It is of interest, in this connection, that Boxer, Pruss, and Goodhart (2) found the pyridoxal phosphate content of leukocytes from human adults to be significantly lower than that of leukocytes from the blood of children and suggested the possibility of regression of leukocyte pyridoxal phosphate content with age.

The existence of a mild state of vitamin B_6 deficiency among the aged is of particular interest, since deficiency of this vitamin has been shown to diminish the absorption of vitamin B_{12} in animals (6) and may bring about adrenal insufficiency (15). It will be of importance to determine whether the adrenal function of old people can be improved with prolonged administration of vitamin B_6.

SUMMARY

SGOT content in sera of healthy individuals was determined and taken as a measure of the state of vitamin B_6 nutrition. It was found that

the concentration of this enzyme in sera of old individuals was lower than in sera of young ones. This agewise difference was found to exist among three groups of young individuals and three groups of old individuals on varied uncontrolled diets.

The SGOT content of the sera of old individuals can be elevated either by the daily administration of 15 mg. of vitamin B_6 per day, or by the addition of pyridoxal phosphate to the sera *in vitro*. The physiological implications of the low SGOT content are discussed.

Elderly individuals were found to excrete significantly more xanthurenic acid in the urine after a tryptophane load test than did young adults. This abnormality could be corrected by the daily oral administration of vitamin B_6.

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AGE CHANGES IN SKINFOLD COMPRESSIBILITY

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In recent years progress has been made in the study of age changes in the gross composition of the body of the living man. A variety of techniques and criteria—body density (3), body water (30), soft-tissue roentgenograms (15)—have been used for the quantification of this important facet of human physique. The applicability of these complex methods is limited to the laboratory and the clinic. In field investigations the direct, somatic measurements of subcutaneous fat, limb circumferences, and bony dimensions (cf. 24) provide useful tools for an approximate analysis of body composition.

Measurements of subcutaneous adipose tissue at various sites may be used, singly, to indicate leanness-fatness at a given site or may be weighed with respect to their intercorrelation and their correlation with body density or total body water as indexes of total body fat. At various sites the skin may be readily folded, with the fold held firmly between the thumb and the index finger. Firm grip, not exceeding the pain threshold, eliminates or at least reduces the variations in the apparent thickness of skinfold that would result from wide differences in the pulling force of the fingers. Calipers are applied at a given distance (1 cm. in our practice) from the fingers by which the skin has been lifted. As the value of the apparent thickness of the skinfold depends on the pressure applied by the calipers, the caliper pressure of 10 Gm./mm.^{2} has been recommended for general use (8) and has generally been accepted (5, 12, 14, 27). This should make possible, within a fairly wide range of shapes and sizes of contact surfaces, the comparison of data obtained by different investigators.

The use of constant pressure calipers, however, has not solved all problems related to caliper pressure. It is, for instance, not known whether there are differences in skinfold compressibility at different sites and at different ages. Skinfolds are composites of skin plus the *panniculus adiposus*. While the decrease with age in the elasticity of the skin itself is well known, the elastic properties of skin-plus-subcutaneous tissue, rich in fat, and their changes with age have not been studied directly.

Compression of skinfolds (skin-plus-fat) has been studied on the basis of comparisons between the values obtained by skinfold calipers (apparent thickness) and the thickness of skin-plus-fat measured on soft-tissue roentgenograms. The agreement between the two methods is fairly close ($r = 0.8$ to 0.9 reported in several studies), but the reported relationship between mean or median values obtained by the two methods is not constant. Garn (13) found pinch caliper values to equal 65% of the true skinfold thickness measured at the level of the lowest rib in the midaxillary line in men (21-22 years old). Brožek and Mori (7) reported mean relative values of skinfolds equal to 84% of the X-ray equivalent measured on the dorsum of the upper arm in men 52-62 years old. Both studies utilized calipers with a constant pressure of 10 Gm./mm.^{2}.

The present study was undertaken to examine directly the problem of potential regional and age differences in skinfold compressibility, utilizing skinfold calipers with pressures of 5, 10, and 20 Gm./mm.^{2}, respectively.

MATERIALS AND METHODS

Skinfolds were measured at the State Mental Hospital, Hastings, Minnesota, on 107 male patients between the ages of 20 and 69 years. In order to obtain a sample relatively homogeneous with respect to physical activity, only those patients who worked for more than three hours a day were included in the study. The goal was to obtain 24 subjects in each of the five decades. Since there was an insufficient number of young patients, three laboratory employees (aged 20, 20, and 22 years) were included. The actual

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We wish to express our appreciation to the Director and Staff of the Hastings State Hospital, Hastings, Minnesota, and especially to Mrs. Helen Williams, Research Council Secretary, for making available to us the subjects needed for the present study (Research Project No. 57-5).

This study was supported, in part, by the U.S. Public Health Service grant H10 (C12).

TABLE 1. MEDIANS OF SKINFOLDS MEASURED WITH 3 CALIPER PRESSURES AT 4 SITES IN 5 AGE GROUPS. MEDIANS, MEANS, AND STANDARD DEVIATIONS FOR ALL AGES COMBINED.

Age group		20-29	30-39	40-49	50-59	60-69	20-69		
Mean age		23.9	34.7	44.4	54.5	64.0	46.4		
N		15	20	24	24	24	107		
Site	Pressure						Median	Mean	S.D.
Arm	5 Gm.	12.6	13.9	9.8	12.4	12.5	12.1	13.2	7.0
	10 Gm.	9.7	12.2	8.6	9.2	10.9	10.0	11.4	6.4
	20 Gm.	8.4	11.0	7.9	8.4	10.1	9.1	10.3	5.9
Calf	5 Gm.	10.7	11.9	6.6	9.4	8.7	9.6	10.5	5.7
	10 Gm.	7.5	10.0	4.8	7.8	7.9	7.6	8.8	5.2
	20 Gm.	6.9	8.4	4.6	6.9	6.9	6.9	7.8	4.7
Scapula	5 Gm.	11.6	19.6	12.3	11.7	13.7	12.9	16.3	9.3
	10 Gm.	9.0	15.6	11.3	10.7	12.2	11.4	14.3	8.8
	20 Gm.	8.4	12.7	10.3	10.0	11.0	10.3	13.0	8.0
Waist	5 Gm.	19.9	21.3	13.9	12.4	15.0	15.2	17.2	9.8
	10 Gm.	15.8	19.1	11.0	11.2	12.9	12.8	15.0	9.2
	20 Gm.	12.1	15.2	9.5	9.8	10.9	10.9	13.1	7.8

TABLE 2. MEAN RELATIVE SKINFOLD THICKNESSES AT 4 SITES IN 5 AGE GROUPS. THE SKINFOLDS MEASURED WITH A PRESSURE OF 10 GM./MM.^{2} AND 20 GM./MM.^{2}, RESPECTIVELY, ARE EXPRESSED AS PERCENTAGES OF THE REFERENCE VALUES OBTAINED WITH THE PRESSURE OF 5 GM./MM.^{2} MEANS, MEDIANS, AND STANDARD DEVIATIONS FOR ALL AGES COMBINED.

Age group		20-29	30-39	40-49	50-59	60-69	20-69		
N		15	20	24	24	24	107		
Site	Relative Pressure						Median	Mean	S.D.
Arm	10 Gm./5 Gm.	83.5	84.4	87.3	84.6	86.6	86.0	85.5	6.3
	20 Gm./5 Gm.	74.7	76.7	79.9	78.0	78.7	77.9	77.9	6.8
Calf	10 Gm./5 Gm.	79.3	83.4	81.6	84.2	82.8	82.3	82.4	9.0
	20 Gm./5 Gm.	69.6	75.5	74.2	75.7	72.1	73.3	73.7	9.2
Scapula	10 Gm./5 Gm.	83.1	85.3	86.8	89.7	89.0	87.4	87.2	8.6
	20 Gm./5 Gm.	74.1	77.3	81.4	81.6	82.1	80.3	79.8	8.5
Waist	10 Gm./5 Gm.	82.7	87.0	84.0	85.3	87.2	86.0	85.4	10.1
	20 Gm./5 Gm.	71.8	74.5	75.5	78.2	77.9	75.4	75.9	9.4

number of individuals in each 10-year age group is given in table 1.

The sites were chosen on the basis of representation of regions known to show large variations in subcutaneous fat and ease of precise location (6). The following sites were used: 1) arm, on the dorsal surface, midway between acromion and the olecranon process; 2) waist, midway between the last rib and the iliac crest in the mid-axillary line; 3) scapula, at the inferior angle of the scapula; 4) calf, at the level of maximum circumference on the medial side of the calf. All measurements were taken on the right side of the body.

The subjects were measured in groups of 10. In each individual the 4 sites were marked with a dermatographic pencil to show (a) the level at which the measurement was to be made, (b) the center of the skinfold ridge, and (c) the width of the skin encompassed between the thumb and the index finger in lifting up the skinfold. The width of the skin pinched varies with the thickness of the subcutaneous fat layer. The width should be minimal, for a given site, still yielding a well-defined fold. For a given man and site the width was rigidly standardized in this study. Three calipers, of the sliding type, reading to 0.1 mm., were used with pressures of 5 Gm./mm.^{2}, 10 Gm./mm.^{2}, and 20 Gm./mm.^{2}, constant throughout the range of skinfold thicknesses. In order to allow the skin to return to its initial state, all 10 men were measured, consecutively and in the same order, with a given caliper. At least ½ hour elapsed between measurements with different calipers. The calipers were used in the order of increasing pressure. The measurements made on each individual were completed within about 2 hours.

The measurements obtained with the pressures of 10 and 20 Gm./mm.^{2}, respectively, when expressed as percentages of the reference values obtained with a 5-Gm. pressure, yield the Relative Skinfold (RS) thicknesses. The

TABLE 3. REGRESSION EQUATIONS ($\hat{Y} = a + bX$) RELATING SKINFOLD COMPRESSION ($\hat{Y}$) AT 4 SITES TO AGE (X) IN YEARS. THE COMPRESSION PERCENTAGES WERE COMPUTED AS 100 LESS RELATIVE SKINFOLD THICKNESS. THE RELATIVE SKINFOLD THICKNESS REFERS TO SKINFOLD MEASUREMENTS MADE WITH A PRESSURE OF 10 GM./MM.^{2} AND 20 GM./MM.^{2}, RESPECTIVELY, EXPRESSED AS PERCENTAGES OF THE REFERENCE VALUES OBTAINED WITH THE PRESSURE OF 5 GM./MM.^{2} N = 107. SE_b = STANDARD ERROR OF THE SLOPES.

	Relative Pressure					
Site	10 Gm./5 Gm.			20 Gm./5 Gm.		
	a	b	SE_b	a	b	SE_b
	(Intercept)	(Slope)		(Intercept)	(Slope)	
Arm	16.52	—0.0427	.0439	25.81	—0.0796	.0472
Calf	19.95	—0.0517	.0626	27.08	—0.0156	.0646
Scapula	18.76	—0.1277	.0593	28.82	—0.1857	.0569
Waist	17.35	—0.0593	.0703	31.65	—0.1635	.0637

TABLE 4. F-TESTS FOR THE SIGNIFICANCE OF THE DEPARTURE FROM LINEARITY OF REGRESSION, AND OF LINEAR AGE TRENDS IN SKINFOLD COMPRESSION.

	Departure from Linearity		Significance of the Slopes (Age Trends)	
Relative Pressure	10 Gm./5 Gm.	20 Gm./5 Gm.	10 Gm./5 Gm.	20 Gm./5 Gm.
Site				
Arm	1.48	1.21	0.95	2.84
Calf	0.83	1.88	0.68	0.06
Scapula	0.98	0.88	4.64*	10.66**
Waist	0.67	1.03	0.71	6.58*
$F_{.05}$	2.71		3.94	
$F_{.01}$	—		6.91	

* Significant at the 5% level.
** Significant at the 1% level.

more compressible the tissue, the smaller will be the relative thickness. The compressibility of the skinfold may be characterized by subtracting the relative skinfold thickness, as percentage, from 100. This yields the Compression Percentage (CP = 100 − RS).

RESULTS

The medians of skinfolds for the 10-year age groups are presented in table 1. It may be noted that there is no progressive age trend in any of these measurements, contrary to the increases one might expect in samples of the general population (3). The reasons for the maximum in the fourth decade (30-39) and its frequent minimum in the fifth decade (40-49) are not obvious. They probably reflect sampling fluctuations and do not invalidate the use of these data for the study of skinfold compressibility.

The mean relative skinfolds are given in table 2. The means seem to increase (compressibility to decrease) slightly with age. For subsequent analysis the relative skinfold (RS) values have been converted to compression percentages by subtracting each relative skinfold value from 100% (CP = 100 − RS).

The equations for the regression of compression percentages on age are presented in table 3. Statistical tests (table 4) were carried out for linearity of regression and for the presence of linear trends (32, p. 278 and 241). In no case did the departure from linearity reach or approach the 5% significance level. The slopes are negative throughout (table 3) but the departure from the horizontal line did not reach the 5% significance level for calf and arm. At the waist, however, the 20 Gm./5 Gm. compression percentages show a linear age decrease significant at the 5% level. At the scapular site the decrease for 10 Gm./5 Gm. pressure is significant at the 5% level, and for the 20 Gm./5 Gm. pressure at the 1% level of confidence. Thus the skin-plus-subcutaneous tissue of the extremities shows less decrease in compressibility with age than do the sites on the trunk.

Significance of the differences between mean compression percentages at the 4 sites was tested separately for each age category and for combinations of age groups. As the compression percentages for the 4 sites were obtained on the same individuals, F tests for correlated variables were applied (4, 25, p. 274). Significant and highly significant differences be-

TABLE 5. F-TESTS FOR THE SIGNIFICANCE BETWEEN MEANS OF COMPRESSION PERCENTAGES AT DIFFERENT SITES IN SEPARATE AGE GROUPS AND IN AGE GROUPS COMBINED.

Age group	20-29	30-39	40-49	50-59	60-69	20-39	40-69	20-69
N	15	20	24	24	24	35	72	107
10/5 pressure	0.71	0.83	3.43*	2.94*	2.14	1.27	6.58***	6.76***
20/5 pressure	1.20	0.56	3.44*	3.16*	5.71**	1.46	11.32***	11.58***
Significance Criteria								
$F_{.05}$	2.84	2.76	2.75	2.75	2.75	2.70	—	—
$F_{.01}$	—	—	4.13	4.13	4.13	—	—	—
$F_{.001}$	—	—	—	—	6.16	—	5.42	5.42

* Significant at the 5% level.
** Significant at the 1% level.
*** Significant at the 0.1% level.

tween sites are present in the 5th, 6th, and 7th decades (see table 5). The differences between mean compression percentages at the 4 sites in the younger (20-39 years) and older (40-69 years) men are indicated graphically in figure 1.

DISCUSSION

Age changes in skin.—Readily observable changes in the skin (9) take place in the normal course of aging. Pathological exaggeration of these normally occurring alterations is seen in "senile elastosis" (33), with its leathery consistency of the skin, and deep, thick wrinkles and furrows, accounted for principally by degenerative changes in the fibrous components of the dermis. Ma and Cowdry (23) reported old age changes in the dermal elastic tissues of biopsy specimens of skin, with a decrease in the amount of elastic tissue and some splitting of elastic fibers. The literature on histological changes in the dermis was recently reviewed by Bensusan (2).

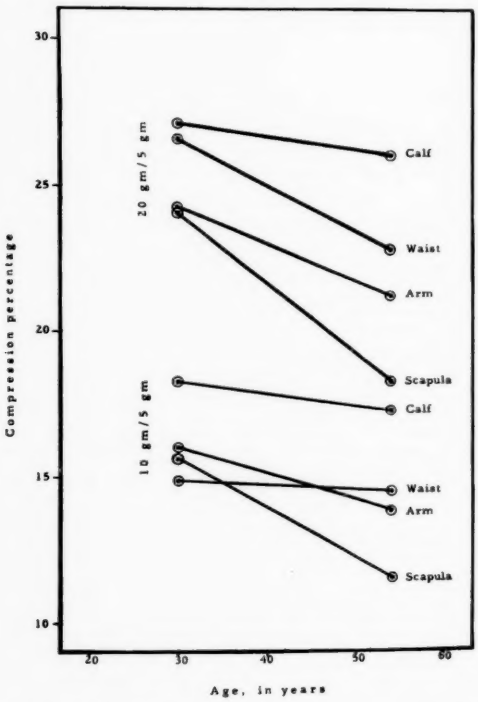

Fig. 1. Mean compression percentages in younger (mean age = 30.1 years) and older (mean age = 54.3 years) men at 4 sites.

Physiological evidence of a decrease in elasticity was obtained by Kirk and Kvorning (20). Four quantities were measured on tracings obtained with the adaption of Schade's apparatus for measuring elasticity of connective tissues (29): 1) the primary indentation, 2) the total indentation (indentation after weight application for 2 minutes), 3) the immediate rebound following the removal of the weight, and 4) the total rebound (the degree of rebound 3 minutes after removal of the weight). For comparative purposes, the magnitude of the immediate indentation and of the immediate and total rebound were expressed as percentages of the total indentation.

The indentation, produced by a constant weight applied to the skin over the medial aspect of the tibia and indicating the compressibility of the tissue, was substantially smaller in their old subjects (60 to 86 years) than in the young subjects (18 to 25 years). The immediate indentation at the upper tibia represented 81% and 64%, respectively, of the total indentation present after two minutes' loading in young and old individuals. The percentage indentations at the lower tibia were 82% and 70%, respectively. The total indentations were 3.5 mm. and 2.2 mm. (upper tibia) and 3.4 mm. and 2.7 mm. (lower tibia) in the young and the old. In addition to these age differences in indentation, which are particularly relevant for

the present study, the degree of immediate recovery upon the removal of the weight, as a measure of the resiliency of the skin, was also much smaller in the elder group. It may be noted that the site used by Kirk and Kvorning is singularly poor in subcutaneous adipose tissue.

In order to investigate the character of the age trends, Chieffi and Kirk performed measurements on a large group of individuals, 148 men and 152 women, between the ages of 25 and 59 years. The data were reported (21) both in tabular and graphic form. The most marked decline with age was observed in the values of the primary rebound (from 56% at 20-25 years to 38% at 55-59, in men; for women the corresponding values were 70 and 44%). In women the skin resiliency, as measured by the immediate and total rebound, is higher throughout the age range.

Strictly speaking only the recovery after the removal of stress is a measure of elasticity, defined as that property of a material which determines the tendency of the stressed material to return to its unstressed geometrical configuration (22). In this paper we have been concerned only with the magnitude of deformation developed in the skin-plus-subcutaneous tissue under varying pressure.

Rollhäuser (28) reported a marked increase with age in the elastic modulus, defined as the ratio of force/deformation, of the human skin. The values rose from 2.9 (young children), to 6.7 (15-30 years), 8.1 (30-50 years), and 11.0 (50-80 years), and indicate that less deformation (in this case stretching) is produced by a given force in the skin of older individuals.

To our knowledge the only dissenting opinion regarding the decrease of the elasticity of the human skin with age is that of Jansen and Rottier (18), who studied the tensile properties of strips of abdominal skin in cadavers and surgical patients, after removal of the subcutaneous adipose tissue. The extension produced by weight varying from 10 to 300 Gm. was recorded. At loads that are more nearly equivalent to the pressure exerted by the skinfold calipers than are the very high loads used by Rollhäuser, the elasticity of the skin appeared to be independent of age.

Compressibility of skinfolds.—In several studies the compression of skin-plus-fat by spring caliper was measured by comparing skinfolds with X-ray measurements. In 65 young men (age 21 to 22) Garn (13, 14) examined the thickness of skin-plus-subcutaneous fat at the level of the lowest rib in the mid-axillary line. The median values for single thickness of fat were 6.0 mm. (skinfold calipers) and 9.3 mm. (roentgenogrammetry), respectively, yielding for the skinfold measurement a relative value of 65% of the uncompressed thickness. Garn noted that it is likely that reduction of the true values by compression (10 Gm./mm.^{2}) is a constant 35% throughout the entire range.

In a study by Brožek and Mori (7), half of the mean skinfold, measured on the dorsum of the upper arm, was 6.5 mm., the corresponding roentgenogrammetric value (after correction for magnification) was 7.7 mm, yielding a relative value of 84%. This value indicates a substantially lower compression (16% vs. Garn's 35%). This discrepancy brought out clearly the need for a further study of regional and other (sex, age) factors that may modify the degree of skinfold compression. The men in the sample studied by Brožek and Mori were in the age range 52 to 62 years, Garn's subjects in the range of 21 to 22 years. The difference is in line with the age decrement in compressibility observed in the present study.

The percentage equivalents of caliper measurements, obtained by using Baker's (1) equation for predicting actual fat thickness, would be 66 and 67% for Garn's median (12.0 mm.) and Brožek's mean (13.0). The subjects included in Garn's study were young men, but neither their age nor the caliper pressure used was reported; the pressure probably was about 5 to 10 Gm./mm.^{2}.

Another equation for converting caliper readings into actual fat thickness was provided by Hammond (17), using data on children obtained with the pressure of 10 Gm./mm.^{2}; the mean age of the subjects was not reported. The calculated equivalents of the 2 skinfolds given in the preceding paragraph would yield relative values of about 57% of the actual fat thickness, i.e., still lower than the values reported by Garn and implying still greater degree of compression.

We cannot offer a straightforward interpretation of the mechanisms underlying the observed changes in skinfold compressibility with age. The authors do not maintain that the differences are accounted for by changed elastic properties of adipose tissue alone. Obviously, skin itself is involved. The hydration of tissues

is likely to vary with age and to affect tissue elasticity. The observed decrease in the compressibility of skinfolds with age may well be due, in part, to a decrease in the water content of the tissues present in the skinfolds reported by Gersh (16).

Regional differences in skinfold compressibility.—In addition to age differences in compressibility of skinfolds, relatively small but statistically significant differences were present in the degree of compression at different sites, with the maximum compression at the calf (17.6% for a pressure of 10 Gm./5 Gm., 26.3% for pressure of 20 Gm./5 Gm.), and the minimum at the scapula (12.8% and 22.2%, respectively). Some explanation of possible regional differences in the compressibility of skinfolds may be found in histological studies.

Dick (10) examined the skin over most of the body. At those sites in which he found thin elastic fibers (medial leg, medial thigh), he later (11) noted that for any given increase of pressure, the excursion of the skin is greater than at those sites (lateral leg, lateral thigh) at which he previously had found thicker elastic fibers. Unfortunately none of our sites other than medial leg were considered in his later study. If his findings on the thigh and leg may be generalized to other areas of the body and are relevant not only for stretching but also for compression, we would expect a lesser degree of skin compression wherever the thicker elastic fibers occur (e.g., the skin of the back).

The fact that regional differences in skinfold compressibility increase with age suggests that the observed age trends in subcutaneous fat (3, 27, 31) are more complicated than might have been assumed. The age changes in skinfold compression complicate also the translation of skinfold thicknesses into total body fat (6, 26), estimated on the basis of body density (19).

SUMMARY

Skinfolds were measured at 4 sites (arm, calf, scapula, waist) in 107 men, 20-69 years of age, using 3 pressures (5, 10, and 20 Gm./mm.^{2}). In each of the 3 calipers, reading to 0.1 mm., the pressure was constant throughout the range of skinfold thicknesses.

Relative skinfolds (RS) were calculated by expressing the thicknesses obtained with the 10 and 20 Gm. pressures as percentages of the 5-Gm.-pressure readings. Compression percentages (CP) were obtained as 100 – RS.

The degree to which skinfolds are compressed by a given pressure decreases with age. The lines portraying the regression of compression percentages on age have negative slopes for both pressure comparisons (10 Gm./5 Gm. and 20 Gm./5 Gm.) and for all 4 sites. The statistical tests indicate the presence of significant age trends for the two trunk sites (scapula and waist).

The range of mean compression percentages for the 4 sites increased with age (3.5 vs. 5.7% for the lighter, 3.0 vs. 7.7% for the heavier pressure). While in the age groups 20-39 years the F-tests yielded no significant differences among the compressibility of skinfolds at different sites, such differences were very marked in the 40-69 year group. Thus, while a decrease with age in the compressibility of skin-plus-subcutaneous tissue is indicated, this decrement is not uniform over the body surface.

The decreased compressibility of skinfolds in older subjects may be expected to exaggerate somewhat the trends toward increase in subcutaneous fat with age described in the literature. Appraisal of the exact magnitude of this distortion and of its changes with age must be based on the comparison of skinfold data with measurements of uncompressed thickness of skin-plus-subcutaneous fat.

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BLOOD PRESSURE, LIPOPROTEINS, AND CORONARY ARTERY DISEASE

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Two biological measurements, blood pressure and serum lipoproteins, have been consistently linked to coronary artery disease. Although the significance of these measures to the disease has been demonstrated quite frequently, there is no more than a qualitative impression of their prognostic value. Gofman (4) introduced an extremely useful method for quantitating these relationships which involved the production of a probability curve from the ordinates of a diseased and a non-diseased distribution. The significance of these probability curves and a method which uses them to measure, in a quantitative fashion, the relationship of a biological measurement to a disease process were recently discussed (6). The purpose of this report is to apply this method to the combination of blood pressure and lipoproteins in coronary artery disease.

Quite generally two groups have been used for comparison: a diseased group (survivors of a myocardial infarction) and a non-diseased group (individuals with no clinical symptoms of coronary disease). Since coronary disease has all the properties of an aging process it is a necessary requisite that these groups be of the same age.

The diseased group should be selected on the basis of the most objective clinical information and not, as is sometimes the case, solely on the basis of electrocardiographic abnormalities. Usually the diseased group represents either successive patients from a cardiologist's practice or a hospital's census. Quite often the measurements are post-infarction measures and as such possibly represent an alteration subsequent to the incident. If blood pressure measurements prior to the incident are available, they have a large probability of being biased because it is not unreasonable to assume that hypertensive individuals will frequent the office of a cardiologist or have reason to undergo blood pressure measurements prior to the incident. A hospital population of coronary infarctions can indeed be different from an at home population.

The non-diseased population should be an unselected population sample drawn from the same population as the diseased group. The use of other hospitalized patients for this sample is not acceptable. The same is true for outpatients of clinics or of a physician's practice. A more realistic approach would be pre-insurance, pre-employment, and periodic physical examinations.

The most reliable sampling is unbiased city sampling, such as is conducted at the Framingham Heart Project (1), where physical examinations with various biological measurements are made. This population is followed throughout life with periodic re-examinations. All measurements thus precede the incident in an unbiased manner and the diseased group grows out of the population sample. The entire time-sequence of events is thus uncovered. It is possible, however, although very doubtful that all the measurements being made will prove to be unrelated. Each new measurement will require a generation to be evaluated.

Retrospective studies have the virtue of being able to yield answers in a short period of time and require a smaller sample of individuals. If we compare a group of 30 to 40-year-old myocardial infarction survivors with a group of non-diseased 30-40-year-olds on a measurement made before the incident, we would have to sample a very large segment of this population to insure a sufficient number in the survivor group. In a retrospective study, this is circumvented; however, a discussion of the possible effects of bias in a retrospective study must accompany the results. Such a discussion should allow one to bracket and closely estimate the results of an unbiased study. Under such circumstances, retrospective studies should become as effective as antecedent studies. In this report, the results of retrospective studies will be discussed through reference to the available data from antecedent studies. The effects of possible bias will accordingly be reduced.

This work was supported by the United States Atomic Energy Commission.

TABLE 1. S_f 0-400 SERUM LIPOPROTEIN CONCENTRATIONS FOR MALES BY DECADES.

Myocardial Infarction Survivors				Group with No Clinical Evidence of Coronary Disease				
Total N	Mean Age	S_f 0-400 Concentration (mg.%)		Total N	Mean Age	S_f 0-400 Concentration (mg.%)		t Test Significance
		Mean	Standard Deviation			Mean	Standard Deviation	
113	45.4	746.1	181.0	1817	44.2	619.4	172.9	0.01
210	54.9	698.2	163.5	1416	54.3	622.5	165.8	0.01
144	63.9	672.9	164.6	402	62.6	609.5	159.3	0.01

Listed in table 1 are the concentrations of the S_f 0-400 serum lipoproteins for a group of male survivors of a myocardial infarction and a group of male subjects who showed no clinical evidence of overt coronary disease. Both groups are subdivided into age groups, and the significance of the t-test of mean differences between the groups in the age groups is recorded. The non-coronary group is composed of the individuals sampled for the Cooperative Study of Lipoproteins (3) and the infarct group represents successive coronary cases from the private practice of participating physicians, the samples having been drawn at least two months post-infarction (2). The report of the Cooperative Study (3) indicates that no bias in the lipoprotein distributions was introduced by this retrospective sampling and also demonstrates the important fact that the lipoprotein elevations seen in table 1 preceded the infarct and were not a result of the infarct.

Listed in table 2 are the proportions of the infarction survivors who have a diastolic pressure above 100 mm. Hg. The data are derived from three sources: (a) The results of the Framingham Heart Project (1), which are designated (F.H.P.), (b) The Donner Laboratories retrospective group listed in table 1, which are designated (D.C.) (2), and (c) An antecedent study by Master (5), which is designated (M.C.). Inspection of table 2 indicates that the coronary cases of the Donner group have shifted to a distribution about lower values of diastolic blood pressure in the post-infarction period. This is in accord with clinical experience. Master's sample is drawn from successive cases of coronary disease in physicians' practices. The blood pressures were obtained prior to the incident. This sample seems to have the same distribution as the more refined sample of the Framingham Heart Project. Again the antecedent studies demonstrate that blood pressure elevation preceded the coronary incident.

TABLE 2. PERCENTAGE OF MALE CORONARY PATIENTS WITH DIASTOLIC BLOOD PRESSURES ABOVE 100 mm. Hg.

D.C.			F.H.P.			M.C.		
Age Range	% Above	Total N	Age Range	% Above	Total N	Age Range	% Above	Total N
40-49	23	113	—	—	—	40-49	26	167
50-59	24	210	45-62	35	51	50-59	32	243
60-69	19	114	—	—	—	60-64	41	63

The foregoing comparisons point up two important facts. One is that the retrospective studies can be as efficient as antecedent studies with such measurements as lipoproteins. The other is that sampling of successive cases of coronary disease from physicians' practices can provide distributions comparable to the more refined sampling techniques. However, it must not be overlooked that it requires the advent of the more refined sampling to prove this point, and if new measures are undertaken, they shall have to undergo this comparison.

The above discussion and comparions apply only to the diseased group, and they do not imply that hospitalized samples are adequate. Such samples require verification, as do the diverse samples of control on non-diseased populations. Actually this is one of the most maligned areas of sampling. The control population should be comparable to the population from which the diseased group has grown. In the report of the Cooperative Study (3) it was demonstrated that the employees of the Los Angeles Civil Service have a cholesterol level which is significantly higher than that of any other sample used in the study. It would be a gross error to use such a sample for comparison of the cholesterol levels of a coronary population drawn from another population. This then practically forces us back to antecedent studies or a demonstration of equivalence.

It can be seen in table 1 that whereas the lipoprotein concentration is essentially constant in the non-coronary population with age, it is decreasing in the coronary population. This is what one would expect if the lipoproteins were a measure of the rate of progression of coronary disease in the population (6). It has

been previously advanced (2) that the lipoproteins are directly proportional to the rate of progression of coronary disease in the population and that $\int$ (lipoproteins) dt is a measure of the amount of accumulated coronary disease. Using the method of calculation of the integral above which was outlined in that report (2), the amount of accumulated coronary disease for the individuals of the Cooperative Study population was calculated. The curves of probability of dying as functions of $\int S_1^{\circ}$ 0-400 dt were developed* and are presented in figure 1. The factor 1/224 used in figure 1 was inserted as an aid to the calculations and is purely arbitrary. Hereafter the value of the integral will be referred to as (T).

It can be seen that the curves for the different ages have the same slope but that their intercepts at 1/(T) equal to zero are different at each age. This is the situation which one would expect if (T) were a measure of an aging process and there were more than one aging process in the disease. These curves at each age are reduced by the mean probability of dying associated with other aging processes in the disease. If there were no other aging process in coronary disease we should expect these curves to superimpose and to extrapolate to unity since the mortality curve for coronary disease extrapolates to unity at infinite time (6).

If (D) represents the death rate at a particular age, then the intercept (I) can be represented as follows: $I = D^{1-x}$, where (x) represents the prognostic efficiency of the measurement. A brief explanation of (x) will follow, but the reader is referred to reference (6) for a more extensive treatment. If two measurements are demonstrated to have an independent relationship to a disease death rate then a population's death date is given by $D = (P_1)(P_2)$, where P_1 and P_2 represent the mean probabilities of dying associated with the respective measures. P_1 can be represented by D^x, then P_2 is given by D^{1-x}. If (x) is 1/2, so is $1 - x$ and the two measures have the same mean probability and are equally predictive. The (x) value for the lipoprotein measurement is shown in table 3. Two values of (x) are given; one for the extrapolated point and one for the last point for which data exist. The extrapolation beyond the point where data exist is obviously in doubt, but these two values bracket the lipo-

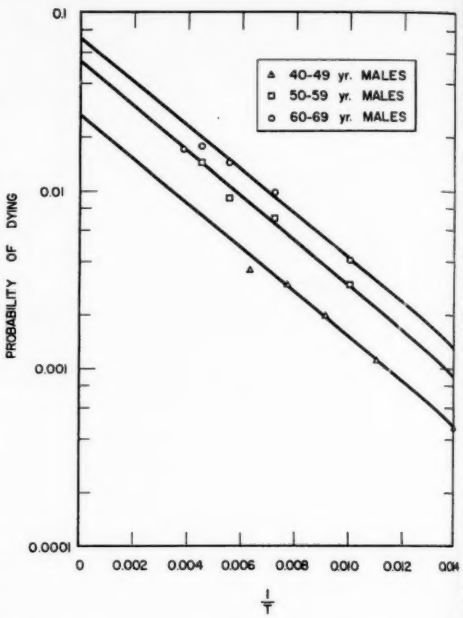

Fig. 1. Probability of dying versus 1/T, where

$$T = \frac{1}{224}\int_0^t S_1^{\circ}0\text{-}400\ dt$$

protein prognostic efficiency. Table 3 indicates that at the very least the lipoproteins account for 1/5 of the prediction of coronary hazard and that there are no more than 4 other variables which are equally as predictive. It also indicates that the lipoproteins may account for 1/2 of the prediction of coronary hazard and that there may be no more than one other measurement which is equally as predictive.

It was demonstrated earlier that the retrospective coronary series cannot be used to develop the probability curve for blood pressure. The available cases of coronary disease from the Cooperative Study are not sufficient to establish a distribution for this purpose. It is possible, however, to construct an approximate probability curve based upon normal distributions which should be close to the facts. The data of Master can be used since they have been demonstrated to be comparable to the Framingham Heart Project data. Master demonstrates that somewhere between 25 and 30% of the coronary population lies above the value

* The method for calculating the probability curves is given in reference 6.

TABLE 3. ANALYSIS OF INTERCEPTS.

Decade	Death Rates*			Predictive Efficiency	
	Actuarial	Data	Extrapolation	Data	Extrapolation
40-49	.0015	.006	.027	.20	.44
50-59	.0055	.015	.054	.19	.44
60-69	.01	.020	.072	.15	.43

* The death rates are obtained by dividing the number dying per year by the number living.

TABLE 4. PREDICTIVE EFFICIENCY IN MALES OF THE COMBINATION OF DIASTOLIC BLOOD PRESSURE AND LIPOPROTEINS IN CORONARY ARTERY DISEASE.

Blood Pressure	Lipoprotein Efficiency		Blood Pressure Efficiency	Combined Efficiency
	Extrapolation	Data		
3.0		.19	.74	.93
2.5	.44	—	.60	1.0
2.5		.19	.60	.79
2.0	.44	—	.47	.91
2.0		.19	.47	.63

of diastolic blood pressure where only 2½% of the non-coronary population exists. Assuming normal distributions and a value of 25%, this would mean that the means of the two distributions are separated by 1.32 standard deviations. Using these figures, blood pressure predictive efficiencies shown in table 4 were calculated. Table 3 gives the predictive efficiency of blood pressure, assuming that 2, 2.5, or 3 standard deviations from the mean was the extrapolated end point. Also listed are the lipoprotein efficiencies for both the data and the extrapolated end-points. The sum of these efficiencies gives the predictive ability of the combination of measurements, and these are listed in the last column. The lowest efficiency in table 4 is 63%, which indicates that at the very least these two measures account for ⅔ of the prognostic capability in coronary disease. Quite obviously these two measures probably account for at least 80% of the predictive capability.

The data of Master further indicate that the mean blood pressure increases with age in both the coronary and non-coronary groups. This is what would be expected if the blood pressure were a measure of an amount of accumulated aging rather than a rate of aging as are the lipoproteins. Therefore the slope of the blood pressure versus probability of dying should be the same at all ages, although the curve for the younger ages will be displaced downward as they are in figure 1. Thus the true probability curve of blood pressure is reduced in the various

TABLE 5. PROBABILITY OF CORONARY DEATH WITHIN ONE YEAR AT VARIOUS S_i^2 0-400 CONCENTRATIONS. AND AGES.

Age Range	S_i^2 0-400 Concentration				T	Probability
	30-39	40-49	50-59	60-69		
	250	200	156	127	75	0.035
	316	254	198	161	95	0.073
	383	308	240	195	115	0.13
	450	361	282	230	135	0.21
	516	415	323	264	155	0.27
	583	469	365	298	175	0.34
	650	520	407	331	195	0.40
	716	574	448	365	215	0.46
	783	627	490	400	235	0.52
	850	681	532	434	255	0.60
	916	735	574	468	275	0.68
	983	789	615	502	295	0.74
	1050	842	656	535	315	0.78
	1116	896	698	569	335	0.82
	1183	949	739	603	355	0.86
	1250	1003	781	637	375	0.90
	1316	1057	823	672	395	0.94
	1383	1111	865	717	415	0.98

age groups by the mean probability of the population due to the lipoprotein-related aging process.

Either of these curves can be converted to the true or absolute probability curve by moving it up until its intercept is equal to unity. The assumption here is that there can be individuals whose probability of dying within one year is equal to unity. Since the coronary death rate extrapolates to unity at infinite age, this reasonable assumption is supported. Using this principle, the data of tables 5 and 6 were calculated. Table 5 lists, for males, the absolute probability of dying for various values of (T). Also presented are the values of the S_i^2 0-400 concentration at several ages which give this value of (T). Since the S_i^2 0-400 concentration measures the rate of accumulation of (T), each higher age requires a lower concentration (slower rate) to arrive at the same value of (T). Table 6 lists the probability of dying attendant to various blood pressure measurements. Since blood pressure seems to measure accumulated aging, this set of values applies for all ages as does the integral value (T) of table 5. The intercept for the lipoproteins was considered to lie between that of the data and the extrapolated point. The intercept for diastolic blood pressure was considered equal to the probability calculated for 3 standard deviations from the non-coronary mean and the curve was smoothed from the 2 standard deviation points to this point. The slope of the blood pressure

curve was obtained by assuming normal distributions.

An individual's coronary disease risk is obtained by multiplying his lipoprotein probability by his blood pressure probability. To test the predictive efficiency of these curves, they were applied to the available sample of the Framingham Heart Project, and death rates (mean probabilities) were calculated for decade groups and compared with actuarial data. These results are listed in table 7. The predictive efficiencies are given in this case by:

$(D_c) = (D_a)^x$ where (D_c) is the calculated death rate, (D_a) is the actuarial death rate, and x is the predictive efficiency.

The predictive efficiency of these curves is essentially 80% in all age groups. The last column in table 7 lists the factor which should be applied to the combined probability to account for, on the average, the missing 20% in efficiency. That is, after one has multiplied the probability from table 5 with that of table 6, this product must be multiplied by the correction factor from table 7.

The authors do not intend to imply that these curves, especially that for blood pressure, be considered any more than working models, and it is hoped that these curves will undergo necessary revision as more data become available from the antecedent studies.

There is not, at this time, sufficient collateral data to allow the same analysis of female coronary risks. Master (5) presents data which indicate that 75% of the female cases of coronary disease arise from that 2.5% of the population whose blood pressures are 2 standard deviations above the mean. This would suggest that in females blood pressure has a prognostic efficiency in excess of 90% and that the lipoprotein process was correspondingly less related. If the probabilities of tables 5 and 6 are applied to the available female population sample of the Framingham Heart Project, the data of table 8 result. The predictive efficiency in females of the data, developed for males, is about 75%, which corresponds to that found for the males. As more data become available this point can be resolved. At any rate, blood pressure is strongly implicated in the females. At the same time, the retrospective studies implicate the lipoproteins as strongly in the females as in the males (2).

TABLE 6. PROBABILITY OF CORONARY DEATH WITHIN ONE YEAR AT VARIOUS LEVELS OF DIASTOLIC BLOOD PRESSURE.

Blood Pressure	Probability
55	0.00096
60	0.0017
65	0.0039
70	0.0050
75	0.0087
80	0.015
85	0.026
90	0.046
95	0.077
100	0.14
105	0.23
110	0.38
115	0.64
120	0.89
125	0.96
130	1.00

TABLE 7. PREDICTIVE EFFICIENCY FOR MALES OF THE CURVES OF TABLES 5 AND 6 IN SEVERAL AGE GROUPS.

Age Range	N	Actuarial Death Rate	Calculated Death Rate	Predictive Efficiency	Correction Factor
30-39	690	0.0004	0.002	0.80	0.2
40-49	703	0.0015	0.007	0.75	0.2
50-59	584	0.005	0.017	0.77	0.3
60-69	192	0.01	0.022	0.82	0.5

The correction factors are given by the ratio of the actuarial death rates over the calculated death rates.

TABLE 8. PREDICTIVE EFFICIENCY FOR FEMALES OF THE CURVES OF TABLES 5 AND 6 IN SEVERAL AGE GROUPS.

Age Range	N	Actuarial Death Rate	Calculated Death Rate	Predictive Efficiency
30-39	874	0.0001	0.0007	0.80
40-49	934	0.0004	0.004	0.70
50-59	757	0.0015	0.018	0.62
60-69	155	0.005	0.018	0.76

DISCUSSION

The authors have not meant to imply or deny any cause and effect relationship between these measures, blood pressure and serum lipoproteins, and coronary artery disease. The intent was only to point up the prognostic ability of the combination of lipoproteins and diastolic blood pressure. The magnitude of their predictive ability has several significant implications.

1. Both blood pressure and lipoproteins are strongly correlated with significant processes in the disease state. Their predictive ability could not be as large as it is unless this were true.

2. Blood pressure and lipoproteins are poorly correlated, and this suggests that each is related to a different process in the disease state.

3. Since the evidence indicates that blood pressure and lipoproteins are strongly corre-

lated with the causative processes, this correlation can be used to uncover the underlying processes.

4. Since these two measures account for 80% of the predictive ability, there remains only 20% to be divided among measures which are not correlated with either blood pressure or lipoproteins.

SUMMARY

Evidence was presented which demonstrates that a combination of lipoproteins and diastolic blood pressure account for 80% of the predictive capability with respect to coronary artery disease. The implications of this finding were discussed.

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6. Tamplin, A. R.: Quantitative Aspects of the Relationship of Biological Measurements to Aging Process. *J. Gerontol., 14:* 134-155, 1959.

BOOK REVIEWS

ARTHRITIS, General Principles, Physical Medicine and Rehabilitation, edited by Edward W. Lowman, Little, Brown and Company, Boston, 1959. 292 pages, $9.50.

This is a much needed book on arthritis for the paramedical rehabilitation personnel. The subjects are covered by authors who are closely associated with the editor, Dr. Loman. This gives the text thoroughness and compactness. However, the book should not be considered an answer to the many questions a physician dealing with rehabilitation of the arthritic patient may have. Also, there are some minor discrepancies. Not everyone today will agree to use muscle "power" loosely as a synonym for muscle "strength." Sequences of joint movements in the act of opening and closing the fist are probably not so fundamental as some of the authors in this book would lead the reader to believe.

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CONGRÈS DE NANCY-VITTEL (25-28 Juin, 1959). Rapports. Association Internationale de Gérontologie, 240 pages, paper bound.

This volume consists of papers presented at a meeting of the European Clinical Section of the International Association of Gerontology which was held in Nancy, France, in June 1959.

The subject matter deals with two major areas of geriatrics—cerebral apoplexy and degenerative skeletal diseases. The majority of the presentations are in French with a sprinkling of German and approximately 10 English papers.

These latter present no new findings in the areas covered but are of interest in that they indicate the clinical thinking and approach of European physicians to some of the medical problems of the aged.

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CONNECTIVE TISSUE, THROMBOSIS AND ATHEROSCLEROSIS, edited by Irving H. Page, Academic Press, Inc., New York, 1959, 316 pages, $9.50.

This monograph is a very valuable publication which deals with those aspects of atherogenesis that are not directly associated with the lipids. It is quite understandable that a great emphasis has been placed on the lipids in the field of atherosclerosis during the last 15 years, but since this has tended to overshadow other possible factors in the pathogenesis of this condition, the review in the present monograph of such other factors assumes particular importance. The book contains an excellent introductory summary by I. H. Page and a review by J. B. Duguid concerning his theory about the development of atherosclerosis. Of the remaining 14 chapters, 9 deal with the different components of the connective tissue and their possible significance in connection with atherogenesis, and in 4 chapters the mechanisms of blood coagulation and fibrinolysis are outlined. In a final chapter by D. Gitlin the subject of immunochemistry and its relationship to atherosclerosis is discussed. Both the presentations and the discussion sections are very well edited, and the book contains many pertinent literature references. Because the monograph supplies so many valuable data related to the possible pathogenesis of atherosclerosis it can be highly recommended to any investigator interested in this subject.

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THE PROCESS OF AGING IN THE NERVOUS SYSTEM, edited by James E. Birren, Henry A. Imus, and William F. Windle. 5th Monograph of "Symposia in Neuroanatomical Sciences." Charles C Thomas, Springfield, 1959, 224 pages, $7.00.

In the process of aging, any organ or organ system may fail first, and such failures may in general affect the functioning of other systems in the interdependent complex of organs making up the organism. The essential problem of this book, not very explicitly stated but everywhere implicit, is to differentiate between the essential or intrinsic changes due to aging of the central nervous system, as contrasted with degenerative changes resulting from nutritional, circulatory, hormonal, or other disease processes in the organs which constitute or determine the physiological and metabolic environment of nerve cells. There is as yet no answer to the question of how old or aging nerve cells would perform in a young and healthy body, and perhaps this problem is insoluble. The secondary problem, of how to keep the nerve cells' environment normal, or even young, is not the concern of this particular study. Yet it is repeatedly made obvious that the differentiation between essential aging processes in nervous tissue and degenerative effects due to more general body conditions is a constant and necessary preoccupation of the discussants. The present status of the problem is that there are no physiological or anatomical changes which can be assigned specifically and solely to an aging process in nerve cells.

Failure of this book to contribute much to the general problems of aging may have an incidental value in the difficulty found in interpreting the results of so narrow an approach. The detailed study of a system *as if* it could be considered independent of others is one necessary approach, but it may not be the most effective in the understanding of the aging process as a whole. Another emphasis suggested repeatedly here, and to some extent under study, is the effect on the nervous system, as the major organ of behavior, of the failure assignable to other organ systems on which it may depend for normal functioning.

The mirror image of aging is the prolongation of youth, the maintenance of efficiency in all functions of the body. The aging process is said to begin at maturity, in whatever sense this implies a peak of effectiveness. This peak seems to be different in the age scale for different organ systems. From the lack so far of any specific identification of an aging process in neurones *per se*, one may infer tentatively that the nervous system

is the last to fail due to age alone, and the capacity of the nervous system to accumulate the results of experience tends to prolong the peak of effectiveness, possibly putting it later than the peak of metabolic or physical functioning. On the other hand behavioral tests indicate a slowing of central response and impairment of complex functions, possibly assignable to deficiencies in the interactions between neurones rather than to changes within them. The last section deals with certain disease conditions which occur more frequently with age, whether or not they can be assigned specifically to an aging process in neurones.

This book is not primarily for the general reader; one will not gain from it much information on how to deal with the vicissitudes of impending senescence. As an attempt to isolate one aspect of a general problem, it presents the status of knowledge for the investigator, chiefly to report the lack of any signal success and to guide further investigation. There is still only one ultimate remedy for old age, and the problem of postponing its denouement encompasses the whole field of human biology.

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VA PROSPECTUS, RESEARCH IN AGING, Veterans Administration, 1959, 125 pages, for sale by the Superintendent of Documents, U. S. Government Printing Office, Washington 25, D. C., $1.50.

To review a symposium such as this involves knowledge of so many fields that one is not likely to find a reviewer who is equally competent in each field and such a reviewer was not found.

The organization of this symposium, aimed at various levels of integration of an organism (the level of the molecule, the cell, the organ, the individual, and the group) is clear, elegant, and refreshing. The authority of the essayists, as well as the discussors, is beyond question. The material presented should be of value to anyone interested in any field of aging. Brief comments on the various presentations may be in order.

Dr. Isidor Gersh's presentation contains a remarkable selection of material from his own and his colleagues' work, including many informative photomicrographs. His own observations are beautifully and modestly interwoven with those of his colleagues. This presentation clearly represents a stride forward in our own thinking about the environment of cells. The notion that certain portions of the ground substance in the neighborhood of cells is "colloid-rich" while other portions of the ground substance are "water-rich" is an engaging one. The discussion by Dr. Griffith and Dr. Lansing and others is more lucid than is usual in symposia, and the extent of the discussion emphasizes the impact of Dr. Gersh's presentation on the audience.

Dr. Robert J. Boucek is concerned with aging at the cellular level. His object of study is connective tissue obtained in the rat by subcutaneous implantation of an inert polyvinyl sponge. This technique provides a sort of tissue culture method in vivo rather than in vitro. Dr. Boucek points out that large amounts of lipids are found in connective tissue and he is very cautious in extrapolating from the connective tissue in the sponge to the connective tissue in the artery.

Dr. Lansing's discussion helps to correlate Dr. Boucek's studies with those of other workers in the field. The exchanges in discussion between Dr. Gerard and Dr. Lansing as to whether aging is at cellular or other levels is particularly intriguing. This leads to some concern about Dr. Boucek's conclusions that "vascular atheromatosis is initiated by an intima irritation, namely the appearance of fibroblasts."

Dr. James E. Birren's essay on aging of organs is confined to the function of the nervous system. His arguments for the notion that slowing down, reduction of speed or response, is not a function of blood flow to the brain or of speed of conduction in a peripheral nerve, but of some disturbance in the central nervous system, is clear and logical. The physiological observations are difficult to controvert. Dr. Gerard's discussion raised the additional issue as to whether speed of response decreased more rapidly with increased complexity of the test. Dr. Birren's reply suggests that this may be so.

The fascinating description by Dr. Geschickter of the variety of rates at which various organs decay and the relation between decay of the various organs and the well-being of the assembled individual leaves little to be desired. His classification of the organs is hard for the reviewer to comprehend. Dr. Geschickter's use of the adjective "secular" leaves me a little confused as to his classification of organs.

Dr. Weinberg's contribution is somewhat beyond my experience. The observations seem only loosely related to aging. Dr. Weinberg emphasizes the fact that symptoms may be inherently *protective*. This reviewer is one of many physicians who do not think of symptoms in these terms.

I should like to include all of Dr. Wilbur C. Davison's summary and Dr. Martin M. Cummings' valedictory in this review but it would be better that the readers turn to the volume itself. For a symposium, it is one of the most coherent that the writer has had an opportunity to attend. The organizers of the symposium are to be congratulated, and the decision to publish was well taken.

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BOOKS RECEIVED

Congrès de Nancy-Vittel (25-28 Juin 1959), Rapports, Association Internationale de Gérontologie, 240 pages, paper bound (Professor R. Herbeuval, 66, Rue des Quatre-Églises, Nancy, France). (Reviewed in this issue, page 58).

The Progress of Aging in the Nervous System, edited by James E. Birren, Henry A. Imus, and William F. Windle, Charles C Thomas, Springfield, Illinois, 1959, 224 pages, $7.00. (Reviewed in this issue, page 58).

VA Prospectus, Research in Aging, Veterans Administration, 1959, 125 pages, for sale by the Superintendent of Documents, U. S. Government Printing Office, Washington 25, D. C., $1.50 (reviewed in this issue, page 59).

General Information

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SECTION B

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2. Papers should rarely exceed 20 typewritten pages, including tables and illustrations. If the total length of a paper when set in type exceeds 8 pages, the authors will be charged the cost of composition and printing for each additional page.
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Publication office is at 1712-24 Chouteau Ave., St. Louis, Missouri. Editorial Offices are at 660 South Kingshighway Blvd., St. Louis 10, Missouri, and Judd Hall, University of Chicago, Chicago 37, Illinois. All communications and remittances relating to subscriptions, back volumes, advertising, etc., should be directed to the office of the Editor-in-Chief, 660 South Kingshighway Blvd., St. Louis 10, Missouri.

Entered as second class matter at the post office of St. Louis, Missouri.

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JOURNAL OF GERONTOLOGY

VOLUME 15, NUMBER 1
JANUARY, 1960

Section B

Psychological and Social Sciences, Social Welfare

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VOLUME 15, SECTION B JANUARY, 1960 NUMBER 1

EGO FUNCTIONS IN THE MIDDLE AND LATER YEARS: A THEMATIC APPERCEPTION STUDY OF NORMAL ADULTS

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Recently advanced concepts in ego psychology have provided a framework for integrating a variety of observations on personality development from infancy to adulthood. These concepts have not yet, however, been systematically extended to personality changes that occur during the middle and later years. Although there are a number of useful references in the literature that relate to modifications in ego functions during adulthood and old age (*e.g.*, Klopfer, 1946; Prados & Fried, 1947; Ames, Learned, Métraux, & Walker, 1954; Caldwell, 1954; Weinberg, 1956; Benedek, 1957), the literature is suggestive rather than definitive. Some of the references are speculative in nature or are limited to observations drawn from psychiatric practice. Among the empirical studies that are relevant, few have been conceptualized explicitly in terms of ego processes; others, based upon samples of institutionalized old people, have produced findings that cannot easily be generalized. In effect, then, empirical findings are fragmentary; and there has not yet been advanced a systematic or generally accepted theory that can serve as a guide for investigations of personality change in adulthood and old age.

It appeared to the present investigators that certain of the concepts developed by ego psychologists, particularly Hartmann (1951), Rapaport (1951), and Lustman (1957), should have direct implications for personality change in the second half of the life span and should lead to testable hypotheses. These concepts may be paraphrased as follows: In the development of personality, the ego has from the first an energy of its own. This energy may be characterized as being highly mobile; and the amount available for coping with stimuli in the external world is highly variable. Excitations from within the organism take precedence over excitations from without; and thus when inner stimuli demand relatively great investment of ego energy, there is less energy available for dealing with stimuli from the outer world. This situation may occur under various conditions. Rapaport (1951) has suggested, for example, several types of interference with the free flow of attention to outer events. Among these are reinforcement of repressed impulses; conditions of fatigue; and the complexity of subject matter to which attention is devoted, with more complex subject matter requiring a change from relatively effortless and involuntary response to effortful and voluntary concentration. It has also been implied (Hartmann, 1951) that available ego energy is diminished by any breakdown in the automatic nature of psychomotor acts.

While they were not originally described as investigations of ego functions, there are a number of empirical studies that suggest a relationship between processes that accompany aging and the establishment of conditions that limit ego functioning. Birren (1955), for example, has described an increase in response latency in psychic as well as in motor acts, and has attributed the time delays to processes within the central nervous system. Another example is the finding (Birren, Allen, & Landau, 1954) that certain intellectual tasks, such as simple arithmetic problems, are more difficult for older than for younger people. This suggests some breakdown in the automatic nature of the behavior elicited by such problems, with the possibility that formerly simple tasks take on a more complex nature for the older person and thus require more voluntary effort.

The decrease in physical energy so often associated with aging provides a probable third condition of interference with the availability of neutralized ego energies. Other biological decrements, such as losses in visual and auditory acuity, place added burdens upon the ego of the aging individual. In addition to such psycho-physiological factors, Weinberg (1956)

has postulated that there is a welling up of unacceptable impulses in the later years which calls upon any available energies for the process of reinforcing repression, thus suggesting still another condition of interference with the outward flow of ego energy.

A constellation of such processes might well constitute inner demands upon the ego of the aging individual sufficient to render the ego less able to maintain its responsiveness to objects and events in the outer environment.

The present research was undertaken in an attempt to follow up relationships between concepts of ego function and empirical findings such as those just described, and in an attempt to provide a more direct test of the hypothesis that with increased age during the middle and later years there is less energy available to the ego for maintaining involvements in the outer world. Certain dimensions of ego function were selected as the investigatory axes of the study, with the postulation that they would provide gross estimates of available "ego energy." These dimensions were: 1) the ability to integrate wide ranges of stimuli; 2) the readiness to perceive or to deal with complicated, challenging, or conflictful situations; 3) the tendency to perceive vigorous and assertive activity; 4) the tendency to perceive or to be concerned with feelings and affects as these play a part in life situations. It was postulated further that these dimensions of ego function would be measurable in projective data, such as those obtained with the Thematic Apperception Test (TAT).

The research steps were, first, to develop methods for measuring these dimensions in TAT data; second, to test the hypothesis that with increasing age, there would be lower ratings on these measures.

THE SAMPLE

The sample was drawn from two larger samples of adults residing in a midwestern metropolitan area. The two larger groups constituted random samples of individuals aged 40 to 71, drawn by modified area-probability techniques, but stratified by sex, age, and socio-economic level. Both large samples had been drawn in connection with the Kansas City Studies of Adult Life; the first, in 1953; the second, in 1955.[1] There was available to the present investigators a pool of 332 persons who had been given an abbreviated form of the TAT. Omitting the persons of lowest socio-economic level, this pool of cases was distributed into 18 cells which varied by sex, by three age categories (40-49, 50-59, and 64-71) and by three social-class categories (upper-middle and above, lower-middle, and upper-lower). Eight cases were then selected at random from each cell.

The present sample thus consists of 144 cases, divided equally on the bases of age, sex, and social class into 18 cells of 8 subjects each. All persons in this sample were living in their own households and were participating in the round of activity characteristic of functioning members of the community. With but a few exceptions, all were persons who had married and raised families and were presently living with their spouses. Of the total 72 males, only three had retired.

METHOD

The data

The data consisted of five stories from each member of the sample given in response to the following cards from the Thematic Apperception Test (Murray, 1943):

Card 1. A young boy is contemplating a violin which rests on a table in front of him.

Card 2. Country scene: in the foreground is a young woman with a book in her hand; in the background a man is working in the fields and an older woman is looking on.

Card 6BM. A short, elderly woman stands with her back turned to a tall, young man. The latter is looking downward with a perplexed expression.

Card 7BM. A gray-haired man is looking at a younger man who is sullenly staring into space.

Card 17BM. A naked man is clinging to a rope. He is in the act of climbing up or down.

These cards were presented to the respondent at the end of an interview that covered various aspects of his present and past life situation. All respondents were interviewed in their own homes or places of business.

[1] The Kansas City Studies of Adult Life, first supported by a grant from the Carnegie Corporation and more recently by Grant No. 3M-9082, National Institute of Mental Health, are being carried out under the direction of Robert J. Havighurst, William E. Henry, and Bernice L. Neugarten. Detailed descriptions of sampling procedures, characteristics of the samples, and methods of estimating social class of respondents are on file as unpublished memoranda with the Committee on Human Development, University of Chicago.

The TAT measures

Four TAT measures were delineated to reflect the personality dimensions of ego-functioning stated earlier. These measures, together with the specific hypotheses to be tested, were:

1. Introduction of non-pictured characters. The hypothesis was that older persons, less frequently than younger, will widen the range of stimuli dealt with by introducing non-pictured characters into their stories. For example, in response to Card 1, the older respondent will tell a story which deals only with the boy; whereas the younger respondent will tell a story in which the boy is interacting with a mother or with some other character not shown in the picture.

2. Introduction of conflict into the story. The hypothesis was that older persons, as compared with younger, would not complicate their story productions by describing intra- or interpersonal situations faced by the characters which involve conflict, choice, or decision. The assumption here was that it requires more ego energy on the part of the respondent to produce a story involving conflict than a story devoid of impeding or controversial elements. For example, in response to Card I, a typical older respondent's story would be one in which the boy is concerned with his adequacy ever to play the violin; whereas a typical younger respondent's story would be about a boy who wishes to please an authority figure by practicing, but who, at the same time, dislikes the violin and does not want to practice.

3. Activity-energy level ascribed to characters. The hypothesis was that older people, less often than younger, would perceive story characters as engaged in vigorous, assertive kinds of activity. This measure was derived from assumptions underlying projective theory regarding the attribution to ambiguous stimuli of one's own underlying tendencies toward movement or action. To illustrate once more from Card 1, a typical older respondent's story might be, "That boy looks like he's falling asleep"; while a typical younger respondent's story might be one in which the boy wants to be outdoors playing baseball rather than indoors practicing the violin.

4. Affect intensity. The hypothesis was that older persons would tell matter-of-fact stories in which little affect is described; whereas younger respondents would tell stories in which various feeling states are elaborated, and in which affect plays a part in the story development. The assumption here was that the description of life situations as being affect-laden reflects a more vigorous involvement with the outer world than does the description of situations as being bland. To illustrate, an older person's story might be, "The boy is looking at the violin, wondering if he can play it." A younger person's story might be, "That boy is angry. He's so angry he'll get up and throw the violin against the wall."

The first two of these measures were rated on a simple two-point scale. A rating of "1" was assigned if non-pictured characters had been introduced into the story; "0," if not. Similarly, "1" indicated that conflict had been introduced into the story; "0," that it had not. "Activity-energy level" was rated on a four-point scale. Since some degree of activity was always present in the stories, the lowest rating assigned was "1." The fourth measure, "affect intensity," was also rated on a four-point scale, but here the lowest rating was "0" because in some stories affective tone was absent altogether.

All the TAT stories were rated blind for age, sex, and social class of the respondent. To avoid halo effect or systematic set, ratings were made separately on each measure, card by card, across the sample. That is, "introduced characters" was rated on Card 1 for all respondents; then on Card 2; and so on. Then "introduced conflict" was rated on Card 1 for all respondents; then on Card 2; and so on.

Reliability of the ratings was checked by selecting at random the protocols of 20 respondents; then, dealing separately with each card and each of the four measures, computing the extent to which two independent judges agreed in rating the stories.[2] On the first two measures there was only one instance in which agreement between the two judges fell below 90 per cent. On the second two measures, coefficients of correlation between the judges' ratings ranged from .68 to .93.

After all ratings had been made, a composite score was computed for each respondent on each measure by simply adding the ratings obtained on the five cards. Thus, the possible range of composite scores was 0 to 5 for "introduced characters;" 0 to 5 for "introduced conflict;" 5 to 20 for "activity-energy level;" and 0 to 15 for "affect intensity."

[2] We are indebted to Mr. Ned Gaylin for his assistance on this task.

FINDINGS

Utilizing the composite scores, a three-way analysis of variance to include the factors of age, sex, and social class was performed for each TAT measure. As shown in Table 1, only the factor of age accounted for a significant portion of the variance on all four measures.

Table 2 shows the mean composite scores on the four TAT measures for the three age groups in the sample. It will be seen that the scores drop from age group to age group on each measure; that the difference between youngest and oldest groups is statistically significant on all four measures; and that, furthermore, in six out of eight instances the difference between adjacent age groups is also statistically significant.

TABLE 1. ANALYSIS OF VARIANCE OF RATINGS ON FOUR TAT MEASURES (N = 144).

Source of Variation	ss	df	ms	F
Introduced characters:				
A	2.78	1	2.78	1.63
B	1.26	2	.63	.37
C	40.26	2	20.13	11.77*
AB	11.01	2	5.51	3.22
AC	1.01	2	.50	.29
BC	6.08	4	1.52	.89
ABC	4.57	4	1.14	.67
Withins	215.25	126	1.71	
Totals	282.22	143		
Introduced conflict:				
A	1.77	1	1.77	1.40
B	3.29	2	1.65	1.31
C	13.79	2	6.90	5.48*
AB	.11	2	.06	.05
AC	1.10	2	.55	.44
BC	4.54	4	1.14	.90
ABC	5.15	4	1.29	1.02
Withins	159.25	126	1.26	
Totals	189.00	143		
Activity-energy:				
A	4.00	1	4.00	1.36
B	15.50	2	7.75	2.64
C	65.29	2	32.65	11.11*
AB	4.67	2	2.34	.80
AC	1.13	2	.57	.19
BC	14.84	4	3.71	1.26
ABC	11.57	4	2.89	.98
Withins	371.00	126	2.94	
Totals	488.00	143		
Affect intensity:				
A	1.77	1	1.77	.27
B	.50	2	.25	.04
C	68.66	2	34.33	5.28*
AB	22.90	2	11.45	1.76
AC	3.57	2	1.79	.28
BC	17.72	4	4.43	.68
ABC	21.63	4	5.41	.83
Withins	819.25	126	6.50	
Totals	956.00	143		

Note.—A = sex; B = social class; C = age.
* Significant at or beyond the .01 level.

DISCUSSION

It had been predicted that with increasing age people would achieve lower ratings on the four TAT measures used in this study. The results were all in the predicted direction: there was a consistent decline with age on all four measures, and the differences between age groups were statistically reliable. As shown in Table 2, the absolute differences between age groups were not dramatic, but in the absence of similar data for younger people, the size of these absolute differences cannot be evaluated.

According to the theory of projective tests, the manner in which people perceive and elaborate upon ambiguous stimuli reveals something of their underlying tendencies to act, whether or not these tendencies are manifest in overt behavior. In keeping with this theory, the age shifts on the TAT measures may be viewed in terms of the more general behavioral tendencies which the measures were designed to reflect. Thus, the findings suggest that older people as compared with younger are less able to integrate wide ranges of stimuli; less able to perceive and deal with complicated or conflictual situations; tend less often to perceive affect as an important part of life situations; and tend toward inactivity or passivity rather than toward more active, assertive forms of behavior.

Since these personality processes had been operationally defined as reflections of ego energy, the differences among the age groups lend support to the hypothesis that with increased age there is less energy available to the ego for responding to, or maintaining former levels of involvement in, the outside world. The implication is that the older person tends to respond to inner rather than to outer stimuli, to withdraw emotional investments, to give up

TABLE 2. MEAN COMPOSITE SCORES ON TAT MEASURES FOR THREE AGE GROUPS.

TAT Measure	Age Group		
	40-49 (N = 48)	50-59 (N = 48)	64-71 (N = 48)
Introduced characters	2.23[a]	1.67[b]	.94[c]
Introduced conflict	3.02[a]	2.38	2.35[c]
Activity-energy	13.19[a]	12.27[b]	11.54[c]
Affect intensity	5.75	5.17[b]	4.08[c]

[a] Applying Tukey's test to the Studentized Range (Snedecor, 1956, pp. 251-252), the difference between means for the youngest and middle age groups is significant at or beyond the .05 level.
[b] The difference between means for the middle and oldest age groups is significant at or beyond the .05 level.
[c] The difference between means for the youngest and oldest age groups is significant at or beyond the .01 level.

self-assertiveness, and to avoid rather than to embrace challenge.

There are findings based upon the Rorschach technique that parallel the present findings (*e.g.*, Klopfer, 1946; Prados & Fried, 1947; Chesrow, Wosika, & Reinitz, 1949; Grossman, Warshawsky, & Hertz, 1951; Davidson & Kruglov, 1952; Light & Amick, 1956). Although there are some inconsistencies in results among the Rorschach studies, it has been inferred from the quantitative findings that older people, as compared with younger, tend to show a decrease in productivity, an impoverishment of the creative intellectual faculties, and a diminished capacity for emotional responsiveness. Light and Amick have stated specifically on the basis of their findings that older adults are "not particularly responsive to stimuli coming from the environment"; that they show a narrowing of social and emotional contacts with others, and a lack of ability to empathize. Such findings may be interpreted as supporting the present hypothesis that with increased age the ego has less energy available for maintaining former levels of responsiveness to outer events.

It is true that the use of projective techniques poses certain problems in the interpretation of age differences. Caldwell (1954), for example, has cautioned against a careless acceptance of the presumed meanings of Rorschach variables developed from investigations of other age groups when evaluating the personalities of older people . She hypothesized that "A certain limen of perceptual flexibility must be crossed before the Rorschach is a valid measure of any significant personality variable in the aged." Although similar caution must be exercised with the TAT, it is nevertheless true that the TAT differs considerably from the Rorschach in this respect. The Rorschach is first and foremost a perceptual test. While a certain degree of perceptual flexibility is unquestionably required on the TAT, this factor is of secondary importance. The subject must be able to perceive the major elements of the stimulus presented on the TAT card; but once this is achieved, the task becomes primarily conceptual. That all the subjects in the present study passed this necessary threshold of perceptual flexibility was evidenced by the fact that the major stimuli were always integrated into the phantasy productions.

As in other studies that deal with psychological differences between age groups, whether or not projective techniques are utilized, there is in the present study the problem of "equivalence of stimuli": that is, whether or not it can be presumed that the stimuli (here, the TAT cards) have approximately the same psychological meaning and significance to subjects of various ages. Although this problem cannot be resolved in a study of this type, it is the investigators' opinion that the findings here reported are somewhat less dependent upon such an assumption than is ordinarily the case. The present analysis rests less upon the specific stimulus value of the TAT pictures than upon ego processes involved in the production of the stories. The variables used here were developed according to a theory of ego functioning; and the TAT pictures were used only as a means of stimulating responses from which these functions could be assessed.

SUMMARY

Abbreviated TAT protocols were analyzed for 144 persons aged 40 to 71, all of whom were functioning members of the community. The sample was divided equally by age, sex, and social class into 18 cells of 8 subjects each. The protocols were rated blind on each of four measures: introduction of non-pictured characters into the stories; introduction of conflict into the stories; activity-energy level ascribed to story characters; and intensity of affect present in the stories. An analysis of variance showed that neither sex nor social class, but only the factor of age, accounted for a significant portion of the variance in the data. The decline in the ratings with increased age of respondent was consistent and statistically reliable for all four measures.

The findings were discussed in relation to the concept of ego energy and its redistribution with age.

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AGE AND PRODUCTIVITY AMONG WORKERS IN FOUR CHICAGO COMPANIES*

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This paper reports part of a larger interdisciplinary study, "Criteria of Aging and Objective Determinants of Retirement," sponsored by the National Institute of Mental Health. The disciplines involved are sociology, psychology, medicine, and economics. This report is based on data gathered in conjunction with the sociological aspect of the project.

The design of the project was based upon a sample of matched pairs of workers in four Chicago companies—a steel mill, a men's clothing factory, a radio and television factory, and a photographic equipment plant. Only white males were used, and each worker must have been on measured incentive production work for a minimum of one year prior to his selection in order to have been included in the sample. One member of each pair of workers was 40-45 years old; the person with whom he was matched was 60-65. Each member of a pair was matched by sex, place of work, occupation, and, depending upon availability of the data, by marital status, ethnicity, and education.

Data on each worker's base pay, bonus, and total income were collected from his company, and the ratio of total income to base income was computed for every worker. This figure was used as an index of relative productivity of each worker when comparisons were made within plants. By comparing these indices it became possible to study the possible relationship between age and productivity for the 132 industrial workers in the sample.

Mean productivity scores

Since there was wide variation between plants in productivity scores, the ratios were analyzed separately for each age group within each plant. Very close similarities were found. At plant A, both the younger and older age groups had mean scores of 1.34. (That is, members of each age group on the average earned 34 per cent of their total pay from the incentive bonus.) At plant B, the mean for the older group was 1.23, while for the younger group it was 1.24, a difference of .01. At plant C the older group averaged 1.13 to the younger group's 1.16, a difference of .03. At plant D, the average score for the older men was .91 and for the younger, .92, a difference of .01. None of these differences is statistically significant.

A comparison of the differences in productivity between members of each matched pair in each plant yielded no significant differences.

Finally, the means for the age groups in the plants were compared by use of an analysis of variance technique developed to measure differences between two samples matched in subgroups on a related trait (Walker & Lev, 1953). Again, no significant differences were found.

It is clear that chronological age is not related to productivity among these workers. Since similar findings have been reported previously (Clay, 1956; King, 1956; Mark, 1956), this lack of relationship, as contrasted with a commonly expected inverse relationship, may be taken as well established.

With these data, as with other data on age and productivity, there are several obstacles in the way of a clear interpretation of the findings. First, these workers were matched according to type of work done. This fact probably means that there was some unmeasured degree of selection in assigning older workers to their jobs. The most able and most physically fit older workers are most likely to continue working on jobs which younger men can handle with relative ease. It is interesting to note in this regard, however, that only one of the four companies had vastly more younger than older workers in the pool from which the selected pairs were drawn.

If problems of pre-selection are ignored for the moment, it may be assumed that there are two opposing effects operating: 1) the differential in physical abilities due to age, and 2) the effects of group norms in limiting output. (The well-known effect of working group norms in controlling output would tend to increase the similarity in production between the two age

* Originally presented at the meetings of the Gerontological Society, Inc., Nov. 6, 1958.
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groups.) There are at least three possible relationships between these effects which may have been operating here: 1) There may be no differences betwen the two age groups. 2) There may be an age effect and a group norm effect which cancel each other out. 3) Finally, there may be no age effect, so that the group norm effect, if it exists at all, operates across the entire age range, thus resulting in no differences between specifically selected age groups. (It should also be noted that other factors besides pre-selection, physical ability, and group norms may be operating. One of these is the worker's attitude toward his job—an attitude which might either reinforce or undermine the age and group effects. The actual *type* of work done is another likely factor.)

Whatever the true relationship between age and group norm effects, one fact is clear from these data. Certain older men, at least, can turn out just as much work as younger men in certain jobs. Since this is true of men aged 60-65 when compared with those aged 40-45, it may also be true of men older than 65, although possibly to a lesser extent. It should be remembered that all of the jobs held by men in this sample involved a certain amount of manual labor. Nevertheless, the older men did quite creditably when compared with the younger men.

Variability

Thus far only one aspect of the productivity of the two age groups has been discussed: the difference between means of the productivity scores. Another important question remains: Is one age group more variable than the other? Do the older men, perhaps because of poorer physical condition, work in spurts of activity and lulls of rest; or are the younger men, perhaps because of less feeling of responsibility to the job, more erratic than the older?

TABLE 1. VARIANCE OF THE SCORES OF OLDER AND YOUNGER WORKERS BY PLANT.

Plant	Age Group	
	60-65 (N = 64)	40-45 (N = 68)
A	.01503	.01359
B	.01428	.01683
C	.00771	.00381
D	.00140	.00180

The data indicate that neither alternative is the case. As with mean scores, there are no significant differences between the variances. Second, when the variability in monthly scores of each worker over one full year was examined, no significant differences between the younger and the older groups were found. Furthermore, there is no pattern to be found in the direction of the differences between variances. In two of the four plants, the older men were more variable than the younger; while in the other two plants the older men were less variable. Thus, neither age group appears to be more erratic than the other.

When the variances of monthly scores of individuals around the yearly score (the latter treated as a mean of the monthly scores) were compared, the same pattern emerged. The test used was Cochran's test (Eisenhart, Hastay, & Wallis, 1947) for homogeneity of a set of variances, a test to discover whether or not the largest variance is significantly out of line with the total.

At plant A, the older group was significantly less homogeneous than chance would allow ($P. < .01$), but the younger group was not. At plant B both groups were significantly heterogeneous (Old, $P < .01$; Young, $P < .05$). At plant C the variances of both groups were significantly heterogeneous (Old, $P < .05$; Young, $P < .01$). At plant D the older group was homogeneous, and the younger group was heterogeneous ($P < .05$). By and large, the variances of individual scores within *both* age groups were more heterogeneous than the operation of chance factors would allow.

Individual variances were then pooled in order to arrive at one variance for each age group. Again, no significant differences were found between the two age groups when *F* ratios were computed. Furthermore, the *pooled* variances for the older group were lower than for the younger group except in one instance. The pooled variances may be treated as arithmetic means as in the computation of a weighted mean, with each set of observations given a weight, added, and the sum divided by the total number of observations.[1] Computation of a *t* test indicated that there were no significant differences between the mean differences in variance of our matched pairs. In plant A, the critical ratio was $-.60$; in B, it was $-.25$; in C, it

[1] We violate one of the criteria for pooling a set of variances when we pool a set of heterogeneous variances. Furthermore, this test does

was −.49; and in D, it was .09. None of these ratios approach statistical significance. Since a complete lack of relationship is shown in an *F* ratio of 1.00, with a *t* ratio of zero, neither of these tests gave a result close to statistical significance. Therefore it may be concluded that the older group is neither more nor less erratic than the other. The older men are just as steady in their output as the younger men.

SUMMARY

In all four plants there were 1) no significant differences in the mean productivity scores between our two age groups; 2) no differences between the variances of the two groups; and 3) no differences between the two groups in the variances of monthly scores of individuals. In short, on these production level jobs, there were no differences between men aged 40-45 and men aged 60-65 in productivity.

not take into account the fact that our sample is one composed of matched pairs. In applying a *t* test to the mean differences in variances for the matched pairs within each plant, we are forced to make no assumptions about homogeneity and we have a test designed to take matching into account. However, it does not take into account the fact that we are dealing with variances. But, if both the pooling test and the *t* tests agree, we may be fairly confident of our findings.

This report clearly indicates the independence of productivity and age in our data, but these findings might also be interpreted with reference to the effects of work-group norms upon production. Since there are no data here on the nature of the work-group situation in the four plants studied, the conclusions expressed in this paper must be interpreted with caution. It may be said, however, that as far as this research project was able to measure the differences, the older group produced as much and as consistently as did the younger group.

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INTERGENERATIONAL FAMILY RELATIONSHIPS AND SOCIAL ROLE CHANGES IN MIDDLE AGE*

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Social roles and family relationships in middle age have been studied by a number of investigators (Deutscher, 1959; Gravatt, 1953; Havighurst, 1957; Neugarten & Gutmann, 1958; Sussman, 1953, 1954, 1955, 1956, 1959). Deutscher found that middle-aged parents tend to define the post-parental situation favorably, particularly those who are involved in many other roles beside that of being a parent. The transition from the child-bearing to the post-parental stage of the life cycle was not perceived as a crisis by the middle-class members of his sample. Havighurst has developed a rating technique for measuring the quality of performance in each of nine social roles. He found no marked decrease in role performance with age in the years from 40 to 70. The higher more than the lower social classes meet role expectations successfully during this post-parental period. Havighurst also points out that social roles can be ordered by the degree of internalization of role expectations. A relatively high degree of internalization of expectations are found in the first-order roles of worker, parent, spouse, and home-maker. The second-order roles are friend and user of leisure time; and the third-order are citizen, church member, and club and association member. The Havighurst data suggest that changes in behavior in all social roles do not occur simultaneously.

THE RESEARCH PROBLEM

In 1957 a study was conducted of the major social roles of a group of middle-aged parents living in the Cleveland metropolitan area whose children had permanently left the parental home. Specifically, an effort was made to discover if relationships between generational families (parents and their married child's family, the latter including the child, child's spouse, and grandchildren) were consistently related to behavior in particular social roles in middle-aged couples; and if middle-aged parents of two different social classes varied significantly in their patterns of social roles as a consequence of the leave-taking of children.

In this study middle-aged parents were defined as couples between the ages 45-60, whose children had married and permanently left the parental home. Generational families are those of the parents and their married child's family. The social roles studied were: parent, spouse, child of aging parents, worker, user of leisure time, church member, club or association member, citizen, friend, aunt or uncle, brother or sister.

THE SAMPLE

A complicated method was followed in an effort to obtain random samples of working- and middle-class families for study. Two separate two per cent random samples were drawn from the list of 12,000 marriages recorded in Cuyahoga County, Ohio, during 1956. Parents were then traced through these married couples, and an effort was made to secure an interview with the parents if they met the criteria of sample selection. These criteria were that the 1956 marriage was of the last child living at home, that the couple were white, and that both parents were between the ages of 45 and 60. Fifty-seven post-parental couples were located in this manner, and constitute the sample for this study.

For the 57 cases the median age of the wife was 53.4 and of the husband, 57.5. Ten of the husbands were in professional or technical occupations; 15 in managerial, office, or proprietary; 5 in clerical and sales; 13, craftsmen or foremen; 14, operatives and kindred workers. Thirty-three were identified as Protestant; 16, Catholic; 7, Jewish; and 1, unknown. Forty-one per cent were natives of Cleveland, and over 75 per cent of the families had lived in the Cleveland area more than 10 years. Approximately one-half of the families represented West European and one-half East Euro-

* This research was facilitated by Public Health Service Grant M 1592 and by a grant-in-aid for research from the Social Science Research Council.

Acknowledgement is made to Mrs. Eleanor Caplan, Research Associate, Department of Sociology, Western Reserve University, and to Miss Mildred Dorr, Family Health Association of Cleveland, for their invaluable assistance.

pean nationality backgrounds. On the average each parental family had two married children. In some instances the last child had married as recently as eight months prior to the interview.

Data were obtained by interviewing one or both members of the post-parental couple. Twenty-two interviews were conducted with both members of the couple present; the remaining 35, with the wife. The time of each interview varied from one and one-half to four hours.

The interviews included structured and semi-structured questions on patterns of inter-generational family continuity and social role behavior.

SOCIAL CLASS AND FAMILY CONTINUITY

The 57 cases were grouped by social class. Class assignments were made on the basis of Hollingshead's Index of Social Position (Hollingshead, 1949; 1954). This index is based upon two factors, occupation and level of education, with a given range of ISP scores representing a given social class. The five social classes delineated by Hollingshead have here been combined into three, with his classes I and II constituting our "upper"; his class III, our "middle"; and his classes IV and V, our "low."

A rating technique was developed to determine the degree of intergenerational family continuity, namely, a measure of the ongoing activities and interpersonal relationships of post-parental couples and their married child's family. The following eight factors were each rated on a three-point scale: 1) Feelings about children's marriage, 2) feelings about child-in-law, 3) closeness of family now, 4) children come for advice and take advice now, 5) family celebrations now, 6) visits between parents and children now, 7) communication between parents and children now, 8) help given to children now.

Scores (summations of the eight ratings) were assigned to one of four levels of family continuity: high, good, fair, or poor. (A fifth possibility, "no family continuity," did not occur in this sample.) The four levels were then grouped into two, "good to high" and "poor to fair"; 36 families were classified in the level called "high," and 21 in the "poor to fair" level, henceforth called "low."[1]

[1] A second method of rating the interviews was used for checking the reliability of the scale. It provided criteria for the raters in judging the level of family continuity and was used initially by the investigator (Sussman, 1953). The correlation between the two methods was .99 by the Spearman rank correlation method.

Social class was found to be inversely correlated with intergenerational family continuity. As shown in Table 1, the higher the class, the lower the continuity.

This finding that high intergenerational family continuity is positively correlated with low social class necessitates re-examination of a much beloved hypothesis, namely, that the higher the social class, the higher the family continuity. This does not mean that previous findings of high continuity among middle class families are to be rejected, but rather that there is need to explore this relationship by further empirical research.

CHANGES IN SOCIAL ROLES

Behavior in each of the 11 social roles mentioned earlier was examined for change since the leave-taking of the last married child from the parental home. A measure of role change was determined by examination of two behavioral items for each role. For instance, investigated under the parent role were changes in advice giving and receiving, and help and service exchanged between parents and children. A typical question was, "Some families help each other out in various ways. Have you happened to give help to your own parents, children, relatives or in-laws?" A similar question was asked about receiving help. The interviewer recorded the types of help exchanged before and since the leave-taking of children. The behavioral item was judged as "change" or "no change" after evaluation of the responses by the investigator.

Each of the other roles was examined in the same fashion with two behavioral items selected as sensitive indices for determining role change. If a couple was reported as "change" on two behavioral items in a given role since the leave-taking of children, then "change" was recorded for that role.

As shown in Table 2, in four of the eleven social roles more than 50 per cent of the couples reported changes since the leave-taking of the last married child. These are the four roles of parent, spouse, user of leisure time, and church member. The frequency of 50 per cent of change in the sample was arbitrarily taken to indicate change in roles. When this measure was used, no significant changes were found to have taken place in the roles of worker, citizen, friend, child of aging parent, aunt or uncle, club or association member, or brother or sister.

Of the four role areas where changes were most frequent, significant differences by social class were found in the roles of spouse and user of leisure time. Significant differences were also found by family continuity levels for the spouse, leisure time, and church member roles.

A significantly higher proportion of couples with poor family continuity, as compared with those of high family continuity, reported changes in spouse roles. Change was in the direction of intensified inter-spousal activity. Couples reported spending more time together and doing more things with one another.

"Middle" and "upper" class parents indicated that spouse roles change before rather than after the marriage of the children. Most of these changes occurred when children went away from home to college. For these couples, the new inter-spousal pattern was well established by the time of the last child's marriage.

The higher the social class, the greater was the change in the role of user of leisure time.

TABLE 1. INTERGENERATIONAL FAMILY CONTINUITY: BY SOCIAL CLASS.

Continuity Level	Social Class		
	High	Middle	Low
Poor to Fair	16	12	8
Good to High	6	2	13

Chi Square 9.754, df 2; $P < .01$.

TABLE 2. NUMBER OF COUPLES WHO REPORTED CHANGES IN SOCIAL ROLES AFTER LAST CHILD LEAVES HOME: BY SOCIAL CLASS, AND BY INTERGENERATIONAL FAMILY CONTINUITY SCORES (N = 57).

Role	Number Who Changed				
	Classes I & II (N = 22)	Class III (N = 14)	Classes IV & V (N = 21)	High Continuity (N = 36)	Low Continuity (N = 21)
Parent	16	10	14	22	18
Spouse	11	13	13[a]	17	20[b]
User of leisure time	16	9	4[a]	9	20[b]
Church member	14	9	12	15	20[b]
Child of aging parents	4	2	4	6	4
Worker	7	3	3	6	7
Club or association member	8	4	6	12	6
Citizen	5	2	3	6	4
Friend	4	3	5	8	4
Aunt or uncle	4	2	3	6	3
Brother or sister	6	5	5	9	7

[a] The differences between social classes are statistically significant at the .05 level.

[b] This difference between high and low continuity groups is significant at the .05 level.

The lower the family continuity, the greater was the change of the role of church member. The direction of change was to become more active in the church.

DISCUSSION

Marriage of a child demands in both a legal and cultural sense that parental roles be redefined. Whether parents are ready or not, they are forced to modify the pattern of interpersonal relationships with their child and his new family. The spouse role is also expected to change quickly. The speed and nature of change is probably related to experience with the leave-taking of children from the family of orientation. If children have attended college, the changes in interpersonal relationships attendant upon the so-called "empty nest" may have begun to change at that time. The marriage of the last child is then the culmination of these changes.

Changes in spouse roles of post-parental couples were most significant among "middle" social class and low continuity families. "Upper" class families indicated that changes in spouse roles commenced during the early adolescence of their children. Many children were sent away to preparatory school and many parents began at that time to note changes in their relationship with one another. "Middle" class more than "lower" class parents indicated significant changes in spouse roles. In part these differences between "lower" and "middle" class couples can be explained by the high family continuity of the "lower" class and low continuity of the "middle" class families in this study.

Both husbands and wives experienced changes as users of leisure time. Substitutes for child-centered activities were those focused on reading, games at home, trips, driving out, hobbies, course taking, television viewing, and sports. Larger blocks of time were now available for home refurnishing, garden work, trips, longer vacations, and for "just loafing."

The "user of leisure time" role varied with social class and with family continuity level. The higher the social class the greater was the change in this role after the leave-taking of children. This change is related to social class values, financial means, and low family continuity. The higher social classes generally have internalized the value of a productive

leisure, and with children no longer underfoot, they have the time and money to pursue the pleasures of leisure. In addition, as a group they spend less time with their married child's family than do persons of the lower classes. This fact has been empirically verified elsewhere (Seeley, 1956; Sussman, 1956). Moreover, more of the higher than lower class parents believed that leisure pursuits should be shared with friends of their own generation rather than with their child's family. It is also relevant that more of the "lower" than "middle" or " upper" class parents had children living in the Cleveland area with whom they could spend their leisure time.

Interest and activity in church may be a carry-over from the Sunday School days of one's children. The change in the role of church member may also reflect the fact that many churches today carry on as many social as religious functions, and thus provide an acceptable channel for the expenditure of leisure time. The leave-taking of children may be the point at which church membership is more eagerly sought than before.

Increased church activity was highly correlated with low family continuity. This may be related to the failure of parents to establish satisfactory social relationships with their married child's family. Another contributory cause, already mentioned, is that a higher proportion of parents with high rather than low family continuity had relatives living within the Cleveland area. The social functions of religious organizations may be a substitute for the lack of social contacts with married children and their families.

The lack of change in worker, citizen, friend, and bilateral kin-related roles might have been anticipated, since these roles are not expected to change as a consequence of a child's marriage. As regards the worker role, for example, only a few of the middle-aged males in this sample changed their occupations or retired when they were relieved of supporting children. More often there was an intensification of work activity by the post-parental male. Mothers more than fathers experienced radical changes in work roles. The interview did not contain questions for quantifying responses concerning changes in homemaker roles, but women respondents reported changes in meal planning, housekeeping, chore load, and shopping. Women now had more time for themselves and for their husbands.

Time is another factor affecting these findings. Some long-established roles may take more than eight months or a year to change, and the leave-taking period studied here may have been too short to test for change in those roles. Data on kin-related roles point to an ongoing network of interaction with nearby relatives that was established long before the leave-taking of children (Sussman, 1959). There are no empirical data to substantiate the belief that post-parental couples become more active than before in social relations with siblings and extended kin. Upon the leave-taking of children, social relations between parents and kin continue in the pre-leave-taking pattern.

Since only four of eleven roles studied showed significant changes in the post-parental period, it can be concluded that radical changes in the lives of parents do not occur immediately upon the leave-taking of children.

In three of the four social roles in which change occurred, differences by family continuity level were significant. In only two of these four were there significant social class differences. It would appear then that intergenerational family continuity is more important than the values and behavior associated with social class in affecting changes in the social roles of post-parental couples.

SUMMARY

Fifty-seven couples aged 45 to 60 were interviewed eight months or more after their last child had married and left the parental home. The couples were studied for the extent to which intergenerational family continuity was maintained, and the extent to which their behavior in each of nine social roles had changed since the leave-taking of the last child. Family continuity was found to be inversely related to social class. Half or more of the couples reported changes in the four roles of parent, spouse, user of leisure time, and church member; but changes in the roles of worker, sibling, child of aging parents, aunt or uncle, club or association member, citizen, or friend, were relatively infrequent. It appears that intergenerational family continuity is a more important factor than social class in affecting changes in social roles among post-parental couples.

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FORMAL CHARACTERISTICS OF HUMAN FIGURE DRAWINGS BY INSTITUTIONALIZED AND NONINSTITUTIONALIZED AGED*

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A comparison of formal indices of human figure drawings by institutionalized aged and by normal children differentiated these two extreme groups. Figures drawn by the children were larger, taller, and more adequately centered on the page than were those drawn by the elderly subjects (Lakin, 1956). This finding may be interpreted as evidence for the theoretical position of Schilder that body image may be understood as a dynamic self conceptual schema based upon interacting and interdependent states of the organism (Schilder, 1935). The finding was also encouraging with regard to the use of the figure drawing as a projective device for investigations in this area (Lorge, Tuckman, & Dunn, 1954). The use of the figure drawing in clinical settings has emphasized its relevance for investigation of body image (Machover, 1948). Hence contrasts in performance on this technique by two such extreme groups as institutionalized aged and normal children would tend to support a theory which emphasizes a dynamic view of body image.

Application of the figure drawing technique seemed useful in studying some of the subtle problems of body image differences among the aged. Increased attention has been focused upon institutionalization and its effects upon the aged. Has a custodial protective environment led to a negatively altered self and body image? In the study of Lakin's cited above (1956), it appeared that the feelings of self devaluation on the part of the institutionalized aged found graphic expression in the execution of formal features of the drawings. However, could it not be that being old in our culture itself gives rise to feelings of futility and worthlessness? If the latter is the case, then no major systematic difference would be expected in a comparison of drawings by institutionalized and noninstitutionalized persons of equivalent age groups.

If aspects of the body images of the subjects are reflected in their drawings, and if the body images of those who are institutionalized differ from those who maintain themselves independently, then group differences in the figure drawings would be expected. The hypothesis is that the direction of difference would reflect the clinically-derived findings regarding human figure drawings; that the institutionalized subjects would express the negatively-toned phenomenal meanings of self-in-an-institution by drawing figures which would be smaller, shorter, and less adequately centered than those drawn by non-institutionalized subjects.

SUBJECTS

Seventy-two individuals, all Eastern or Central European Jews, served as subjects for this study. Half of the subjects had been residents in homes for the aged for periods of from one to five years; the other half were retired or semi-retired persons who lived independently or "roomed in" with their own or with other families and who were members of Golden Age Clubs. Known psychiatric cases were excluded. The individuals of both groups were ambulatory and judged to be in good contact with reality at the time of the present investigation. The educational level of the two groups was comparable, although secular educational background was minimal for both. Artistic experience or training in drawing was not a factor which differentiated the groups. Data regarding the subjects are summarized in Table 1.

METHOD

The institutionalized subjects were administered the figure drawing task in individual examination sessions. Directions were limited to the simple statement, "Draw a person; you may make it any way you wish but be sure to draw

Presented at the American Psychological Association meetings, September, 1959. This investigation was supported in part by Duke University Regional Center for the Study of Aging, which is supported by the National Institute of Mental Health and the National Heart Institute.

Thanks are due the staffs of the Drexel Home for the Aged, the BM2 Orthodox Jewish Home for the Aged, and the Jewish Community Centers' Golden Age Clubs of Chicago for their cooperation in this study. The author is also grateful to Dr. M. A. Lieberman of the University of Chicago for his aid.

a whole person, not just the face." Noninstitutionalized subjects were given identical instructions but were given the task in group settings, as they came together for a regular club meeting.

Measurement of the formal indices of the drawings which were to be compared for the two groups and the scoring methods were as follows:

Area. The area of each drawing was measured by a geographer's planimeter. This instrument yields results in terms of square inches. The number of square inches covered by the drawing was the score.

Figure Height. The distance from the top of the figure to the bottom was measured with an ordinary ruler. The height to the nearest inch was the score.

Centeredness. A grid-template of concentric circles one-fourth inch apart was placed over the sheet in order to measure the distance from the center of the sheet to the center of gravity of the figure (the midpoint between the figure's extremities). The distance from the center of the sheet to the center of the figure was the score.

Analysis of variance technique was employed in order to evaluate the differences between institutionalized and noninstitutionalized subjects and between the age categories represented in each group.

RESULTS

Table 2 shows the result of the analysis of variance for the dimensions of area, height, and centeredness.

Differences between these two groups of aged were significant on each dimension. Noninstitutionalized individuals drew larger, taller, and more adequately centered figures than did the institutionalized. Age was not a differentiating factor.

TABLE 1. THE SAMPLE.

Group	Males	Females	Age		
			67-74	75-80	80-85
Institutionalized (N = 36)	16	20	12	12	12
Noninstitutionalized (N = 36)	21	15	12	12	12

DISCUSSION

Institutionalization is a multidetermined procedure based upon considerations such as physical illness, inadequate finances, inability, unwillingness or unavailability of next-of-kin to assume the care of the aged individual, and extreme loneliness. Admissions were all voluntary in the cases of the institutionalized subjects. The "Golden Age" group members who maintained a quasi-independent, extra-institutional existence were similar to the institutionalized subjects in most respects. In fact, a number of these persons had applied for admission to the homes on the basis of the considerations listed above and were being considered for admission. It cannot be stated definitively that no differences exist *a priori* between self concepts and body images of those persons who seek admission to a home for the aged and those who do not. Nevertheless, it would seem that practical considerations governed the request for and the grant of admission in the cases of the institutionalized subjects. On this basis disparity between body images of the two groups might not have been anticipated.

The focal issue is that of the effects of institutionalization upon body image as an aspect of self concept. To investigate this issue is not to question the social value of custodial care. For example, prolonged hospitalization may have deleterious psychological effects despite the objective necessity for such care for persons of any age. The striking discrepancies between institutional procedures aimed at benefiting the

TABLE 2. ANALYSIS OF VARIANCE OF DIFFERENCES IN THE FIGURE DRAWINGS.

Source of Variation	Sums of Squares	*df*	Mean Square	*F*
A: Area				
Within	1444.0	66	21.9	
Groups	440.0	1	440.0	29.09*
Ages	1.6	2	.8	.37
Interaction	2.4	2	1.2	.55
B: Height				
Within	195.0	66	2.9	
Groups	53.3	1	53.3	18.06*
Ages	3.5	2	1.7	.59
Interaction	3.7	2	1.8	.63
C: Centeredness				
Within	1191.0	66	18.0	
Groups	288.0	1	288.0	15.96*
Ages	55.0	2	27.5	1.52
Interaction	160.0	2	50.0	2.77

* $P < .01$.

"client" and, on the other hand, the "client's" experience of degradation, loss of self esteem and alienation from people "on the outside" have been dramatically described by Goffman in the cases of mental institutional settings (Goffman, 1959). May it be that similar discrepancies obtain for institutionalized aged?

It seems likely that the protective environment of the homes for the aged, notwithstanding the demonstrated and unquestioned concern for the client's welfare, acts to exacerbate feelings of personal insignificance and of relative impotence. Conversely, independent or quasi-independent functioning in the mainstream of society apparently sustains an individual in the belief that he remains a person of some significance and maintains a degree of control over his own destiny.

The figure drawing technique may continue to prove useful in furthering our understanding of other problems in this area. Emphasis upon the formal aspects of the drawings should minimize the problems of differential educational and training level of subjects, problems for the investigator who endeavors to study the drawings qualitatively.

The present findings suggest that change in the personal environment may have great psychological consequences in later years in terms of body-image. Presumably, positive as well as negative alterations in body-image may be evaluated through application of similar methods. In what ways might institutional structure and/or activity be altered in order to sustain self concept and benefit body-image? What effects might be produced on body image in the aged by means of the various therapies; individual, group, drug, and somatic? What occurs in terms of body-image change for that aged individual who maintains an extra-institutional existence beyond a point of diminished reality orientation?

Investigation of these questions through the proposed or similar methods would have considerable practical as well as theoretical significance for the problem of self concept and body image among the aged.

The perception of personal status in relationship to the interaction of social institutions and the self, and the consequent effects upon body image, constitute a major area for gerontological investigation at the present time.

SUMMARY

In order to evaluate the hypothesis that the perception of alteration in life status is reflected in figure drawings, the drawings of two groups of aged persons, 36 institutionalized and 36 noninstitutionalized, were measured quantitatively. The two groups were comparable with respect to other relevant factors. The drawings by the institutionalized aged were more constricted, shorter, and less adequately centered. Age was shown to be an insignificant factor. The present study thus indicates that change in perception of life status, but not age itself, has a major effect upon alteration in body image as reflected in figure drawings. The technique might be employed in further investigation of the effects of planned modifications (such as therapies, or activity programs) upon self concept and body image.

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AGE DIFFERENCES IN INCIDENTAL AND INTENTIONAL LEARNING*

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There can be little doubt that there is in general a decline in learning ability in old age (Gilbert, 1935, 1941; Gladis & Braun, 1958; Korchin & Basowitz, 1957; Ruch, 1934a; Thorndike, Bregman, Tilton, & Woodyard, 1928). The reason for the decline, however, is less clear. Three main explanations have received attention in the past, the most prominent of which are the "plasticity" theory and the theory of disuse. A third, which has received relatively little attention, involves a decline in motivation to learn, or in attention.

Plasticity theory attributes the decline in learning ability to decreased modifiability of the nervous system. According to this theory, since learning is basically some physical alteration in structure in the brain, and age is generally acknowledged to be accompanied by a slowing down of physical processes, decreased speed of physical change must be responsible for the loss in learning ability. Thorndike *et al.* (1928), Ruch (1934a, 1934b), and Hebb (1942) are among those who have discussed this hypothesis. The work of Ruch (1934a) and Korchin and Basowitz (1957) support the plasticity theory, indicating that there is a greater age loss for less familiar materials, a finding consistent with the prediction the plasticity theorist would make that more familiar materials, presumably requiring less extensive structural changes in the nervous system, would consequently be less difficult for the aged to learn.

The second major explanation for the loss in learning ability is "disuse," a lack of practice in learning situations by the older subject. Thorndike *et al.* (1928) came to consider disuse to be an important factor, although they had at first apparently held to plasticity theory exclusively. Just how this effect would occur is not made clear, in terms of learning theory, and at first sight it might suggest that the writers who use this explanation are thinking of a discrete faculty which must be exercised in order to maintain its vigor. More recent work, however, such as Harlow's (1949) on learning sets, shows that such an explanation must be taken seriously whether or not the mechanism is understood. If "learning how to learn" occurs, it seems clearly possible that forgetting how to learn may occur as well. However, though Sorenson's work (1930) may be used to support the application of a theory of disuse of the aged, Husband's work (1930) provides some evidence to the contrary. Thus, there is little evidence to support the theory at present.

The third general explanation is loss of motivation or attention. McGeoch and Irion (1952), for example, suggest that the aged may learn more slowly because of lower motivation to learn. The importance of such a factor for the age decline has yet to be demonstrated, however, and there is little relevant experimental work to support it.

A comparison of the incidental and intentional learning performance of young and old learners might be highly informative in evaluating the above theories. Either a theory of disuse or a plasticity theory should lead to the prediction that the old subject should perform more poorly than the young under both conditions of instruction, with approximately the same relative difference in performance obtaining between intentional and incidental learners within each of the two age groups. However, a theory based upon an age loss in motivation or attention should lead to the prediction (A) that old intentional and incidental learners should differ less than young incidentals and intentionals; and (B) that the greatest difference between young and old learners should occur under the intentional condition, since the effects of age differences in motivation or attention should be minimized under the incidental condition.

Studies of incidental learning have been conducted by Bromley (1958), Jones, Conrad, and Horn (1928), Willoughby (1927, 1929), and Speakman (1954). The first three might be taken to indicate that there is an age loss under incidental conditions, while Speakman's results suggest that there is none. Unfortunately,

* This study was supported by a research grant from the Canadian Department of Veterans Affairs, Project 14-56, to Dr. D. O. Hebb.
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no study included both incidental and intentional conditions for the same material. The present paper is a report of such an experiment.

METHOD

Subjects. The subjects used were 17 males over 65 (mean age, 71.9 years) and 20 males aged 18 to 29 (mean age, 20.3 years). The young subjects were college sophomores. The older group consisted of subjects obtained from various sources: ten were college professors or prominent ministers, while the other seven were patients at a veterans' hospital or were residents in a veterans' custodial home. Originally, it was intended that an older group consisting entirely of professional persons should be used for comparisons with the young college group, on the assumption that they should be comparable in intellectual level, if not superior, to the younger group. When only ten professional subjects could be obtained, however, the sample was enlarged by highly selective sampling from a veterans' hospital and a veterans' custodial home. Evidence will be given later to show that the older lay and professional subjects were in fact comparable in learning ability, and that combining the two groups was legitimate.

Materials. Six words were printed separately on six plain five- by eight-inch index cards. Each word was printed in a different color in letters one inch high and one-half inch wide. The words used were: *middle, agile, gloomy, sturdy, cautious,* and *wicked.* They were printed in leaf green, red, yellow, turquoise, orange, and violet, respectively.

Design. Subjects were assigned alternately to the intentional and incidental conditions. All subjects were told that they were to take part in an experiment concerned with the effect of word color on reading speed, and were asked to read each word as rapidly as possible. In addition, intentional subjects were informed that they would be tested afterward for knowledge of the specific color in which each word was printed.

The method of presentation consisted of holding up each card in turn, by hand. The card was removed as soon as the subject pronounced the word printed thereon. Following presentation of a sample card, the series of six cards was presented six times in succession. The experimenter recorded response times by means of a stop watch to increase the credibility of the covering task for the incidental subjects and to emphasize the importance of fast response for the intentional subjects.

Next, all subjects were tested for recall of the word-color relationship. Six large illustration boards, each of which contained one of the six words printed six different times in the six different colors, were presented to the subjects. The subjects were requested to identify the color in which each word appeared during the reading test. The subjects' scores were the number of correct recognitions.

Following completion of the recognition test, all subjects were tested for normal color vision by means of a standard test [Pseudo-isochromatic plates for testing color perception (Revised selection), American Optical Co., New York, 1940]. Those who failed to score within the normal range were then eliminated.

This procedure resulted in the loss of five subjects. The final group consisted of 15 older subjects and 17 younger subjects. Nine of the older subjects were intentional learners and 6 were incidental learners. Seven of the younger subjects were intentional learners and 10 were incidental learners. There were 16 intentional subjects and 16 incidental subjects.

All subjects were next assigned the task of learning a series of seven paired associates under intentional instructions. A rank-order correlation coefficient (rho) was computed between number of correct recognitions of the word-color task and number of trials to learn the list of paired associates for those subjects who were under intentional instructions on both tasks. The value obtained was + 0.79. Comparison of the young intentionals and incidentals on number of trials to learn the paired associates task using the Mann-Whitney test produced a normal deviate (z) of 1.27, while a similar comparison for the old intentional and incidental groups produced a z of 1.96. The first difference is not significant, while the second one is. However, since the older incidental group was the poorer of the two, this can only serve to increase the credibility of the findings to be reported. Comparison of the old lay and professional subjects resulted in a z of 1.05, which is not significant. The importance of this subsequent testing for the present experiment is that it provides evidence that the results to be reported cannot be attributed to failure to equate the intentional and incidental groups

for learning ability, and that the old professional and lay subjects (mentioned earlier) were comparable.

RESULTS

The median color recognition scores are presented in Table 1. The median score of the young intentional group was superior to that of all other groups, but none of the remaining groups differed significantly from one another. The Mann-Whitney test was used to evaluate the significance of all group differences. The normal deviates (z's) and levels of significance resulting from these tests are also presented in Table 1.

DISCUSSION

The results indicate that in the absence of instruction to learn there was no age difference in the amount of learning which occurred. While the performance of young subjects improved under the condition of instruction to learn, the performance of old subjects did not, so that a significant difference between the intentional learning performance of young and old subjects resulted.

It should be pointed out that it does not follow that there is no age loss in learning under incidental conditions, for there is no assurance that old and young subjects would have performed at the same level had they all been tested at the same age. (A longitudinal study would be the only sure way of providing evidence to support such an assertion.) Thus, the findings of no age difference in amount learned between the incidental groups does not at one stroke eliminate the theory of disuse and the plasticity theory. Failure to obtain a difference between the old intentional and incidental groups does, however, render these theories implausible as the *sole* factors involved in the age decline.

Aside from the obvious conclusion that some other factor or factors must be involved, perhaps of a motivational or attentional nature, very little can be said. Any further statement hinges on the ability to make statements about how intentional and incidental instructions produce their differential effects on the learner's performance. What one considers the source of the effect is, at the present time, a matter of personal preference. Under intentional instructions, the learner is presumably set *or* motivated to respond to a limited set of environmental events. Under incidental instructions, motivation or set to learn is considered to be minimal, unfocused, and nonspecific.

Experimentation on the age decline in learning ability has been concentrated largely on the effect of variations of the type of material to be learned. Other areas that need investigation include variations in instructions (as in the present experiment), variations in incentives offered the learner, and measurement of physiological changes in level of arousal during various learning conditions.

TABLE 1. MEDIAN COLOR RECOGNITION SCORES.

Subjects	Intentional	Incidental	Mann-Whitney test (z)
Young	6	3.5	2.29*
Old	3	3	0.42
Mann-Whitney test (z)	2.17*	0.68	

* Significant at or beyond the .05 level.

SUMMARY

Fifteen subjects over 65 and 17 subjects under 30 learned a word-color relationship under either incidental or intentional learning conditions. There was a significant age loss in amount learned under the intentional condition, but no difference was found under the incidental condition. While young intentional and incidental subjects differed in amount learned, there was no difference between the old intentional and incidental subjects, a finding which led to the suggestion that the theory of disuse and the plasticity theory are inadequate as complete explanations of the decline in learning ability with age. Other factors, perhaps motivational or attentional, are suggested.

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AGE DIFFERENCES IN THE ACQUISITION AND EXTINCTION OF THE GSR

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This investigation included a comparison between subjects in two age groups with respect to the number of trials necessary to condition and extinguish the Galvanic Skin Response (GSR). It has been suggested that the GSR, as a measure of sympathetic activity, can be a useful index of general level of activation or reactivity (Woodworth & Schlosberg, 1954, pp. 133-144). Thus the present data provide a basis to infer possible age differences in reactivity. The need for data of psychophysiological reactivity in relation to normal aging has been desribed in a recent review of the literature (Botwinick, 1959).

METHOD

Subjects. Subjects of this study were 48 male volunteers of two age groups. The older group comprised 39 subjects who were found generally "healthy" by medical screening. Upon further detailed medical observation, however, 16 of these subjects were found to have noninterfering ailments of varied or mixed types while the remaining 23 elderly subjects were without apparent disease of any kind.[1] These subgroups had mean ages of approximately 73 and 71 years respectively, and will be referred to as "Mixed" and "Normal." The younger group (mean age, 20 years) comprised 9 religious volunteer subjects who were quartered for research purposes in a Clinical Center NIH ward. Other members of the group of which the younger subjects are part were not found different from a group of college students on various psychomotor tests. The 9 subjects were without apparent disease.

Procedure. All GSR recordings were made with a Fels dermohmmeter and Fels electrodes attached to the soles of the feet of the subject in supine position. The electrode was a plastic cup 2 cm. in diameter with a zinc bottom. Each cup was filled with electrode paste prior to use.

The general procedure was to present the subject with three consecutive shocks to familiarize him with the unconditioned stimulus (US). Following this, a tone was presented for as many trials as necessary to extinguish the GSR. Extinction was carried out to a criterion of 4 out of 5 consecutive trials. Each subject was then given 15 pairings of the tone (CS) and US which were separated by approximately 4 seconds.

The CS was a 450-c.p.s. tone of 65-70 db intensity that was presented for 0.5 second. The US, applied for 0.1 second to the index and fourth fingers of one hand, was a current of approximately 1.1 ma. The only instructions given to the subject were some variations of: "Just to have you become familiar with what you might expect, we will give you one stimulation on your fingers and then we will start the experiment. Your main job is to lie back and relax. I'll tell you when you will receive the stimulation. All right, now!"

The only purpose of the instructions was to reduce tensions and familiarize the subject with the shock stimulus. Subjects were not informed of the purpose of the experiment and verbal interaction occurred only when necessary.[2]

RESULTS AND DISCUSSION

It may be seen in Table 1 that elderly subjects conditioned less readily than did younger subjects. In addition, the elderly subjects extinguished more readily to the tone that was presented prior to pairing with shock ($p < .05$-$.01$). Although elderly "Normal" and "Mixed" subgroups were not statistically different in these respects, the "Normal" elderly subjects differed from young subjects in both measures while the "Mixed" subjects were statistically different only in the rate of extinction prior to conditioning. All tests in this study were made with both the Mann-Whitney "U" test (Mann & Whitney, 1947) and the parametric t-test. The two tests gave similar results. It may be seen in Table 1 that individual variation (σ)

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[1] The elderly subjects of this study were examined thoroughly in the course of an interdisciplinary study by several NIMH investigators, with Dr. James E. Birren, Section on Aging, as principal coordinator.

[2] The investigators wish to thank Mr. Samuel Umberger for his assistance in the collection of the data, and Mr. Joseph S. Robbin for his assistance in the computation of the results.

was large in spite of the significant age differences.

To the extent that the GSR is accepted as an appropriate index of level of activation or reactivity, it must be concluded that the older group was not as reactive as the younger group. This conclusion was strengthened when approximately one-third of the elderly subjects who tended to be low in responsiveness were given an additional 15 conditioning trials with either a stronger US (1.65 ma.), instructions emphasizing the temporal association between US and CS, or both. Although this increased the reactivity scores, essentially the same age difference result as in Table 1 was found between the total elderly sample and the young one.

Activation or reactivity appears to be a general process rather than one that is solely dependent upon the specific experimental procedure. When for the total sample the extinction measures *prior* to conditioning were correlated with the number of CR's during the 15 trials, the coefficient of correlation (r) was found to be .62 and the correlation ratio (η) was found to be .71, indicating that these measures share more than one third of the common variance. Extinction *after* conditioning showed a similar result. Following the conditioning procedure, subjects were extinguished to a criterion of 4 out of 5 trials. Correlations between the number of these extinction trials and either the number of CR's during the 15 conditioning trials, or the number of trials prior to conditioning, were also approximately .60 as determined by r and more than this as determined by η. Even with the additional conditioning trials for several of the elderly subjects, the "Normal" older group extinguished more rapidly than did the young group ($p < .05$). The "Mixed" group, however, was not statistically different from the young group. When elderly and young subjects were equated on their measures of initial extinction, conditioning, or final extinction, and then tested on one or the other of the two measures, no age differences were found in these cases ($p > .05$). This was taken also to indicate that reactivity level is a general characteristic of the individual.

In a recent study, Braun and Geiselhart (1959) investigated eyelid conditioning of male subjects in three age groups. They also found that conditioning rate decreased in advanced age. In explaining their data, they rejected a Pavlovian report that "liveliness of the nerve processes" decreases with advanced age and, instead, suggested an adaptation hypothesis. They suggested that "in the course of many years of living, the eyelid response as well as probably other responses have been 'adapted out' and thus less susceptible to subsequent conditioning" (1959, p. 388). The hypothesis of reduced nervous system excitability was rejected on the basis of data which suggest that activation time of the eye remains unchanged with age, and on the basis that they did not find a significant age difference in the latency of the CR.

One would think that the asymptote of the "adapting out" process would occur early in life—perhaps by young adulthood or even earlier. Nevertheless, if the eye blink, the GSR, and other reflexes are "adapted out" in advanced age, then the argument for some kind of reduced behavioral reactivity is strengthened. The possibility of neural reactivity or excitability, however, remains open and deserving of further investigation. It is important to note that the elderly are less reactive than the young with a reflex that is, potentially, under voluntary control (eye blink), as well as a reflex which involves the autonomic nervous system (GSR).

TABLE 1. AGE DIFFERENCES IN FREQUENCY OF GSR TO A TONE BEFORE AND DURING CONDITIONING.

	Number of Trials to Extinguish GSR Before Conditioning			Number of CR's During 15 Conditioning Trials		
	Mean	Median	σ	Mean	Median	σ
Elderly† (N = 39)	11.9**	8.0	9.6	5.9*	6.0	5.0
"Normal" (N = 23)	11.4**	7.0	8.8	5.5*	6.0	5.0
"Mixed" (N = 16)	12.8*	8.0	10.9	6.4	6.0	5.2
Young (N = 9)	22.9	23.0	12.6	9.9	11.0	4.5

* Significantly different from young group at < .05 level.
** Significantly different from young group at < .01 level.
† "Normal" and "Mixed" elderly subjects are not different, $p > .05$.

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A RESEARCH NOTE ON THE KNOX CUBES AS AN INTELLIGENCE TEST FOR AGED MALES

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In the author's experience, the most commonly used test of general ability, the WAIS (Wechsler, 1955) is not the most suitable for use with older persons, among other reasons because it takes too long to administer. In evaluating various intelligence test items for use in differential diagnosis of the aged, we have been experimenting with the Knox Cubes, using the Arthur adaptation of the test (Arthur, 1947), and are here reporting our preliminary findings. The test materials consist of four one-inch brown cubes, two inches apart, fastened to a thin board. The examiner, following a predetermined order, taps the four cubes with a fifth cube at the rate of one per second. He then asks the subject to do likewise. The tapping series increase in length and progressively become more difficult. The test is discontinued after three consecutive failures.

The writer is not aware of Knox Cubes being used previously in any experimental work with the aged. There are references, however, to work done with children. The Knox Cubes were originally devised (Knox, 1914) as part of a battery of performance tests roughly standardized as an age scale. The original test had series and norms for ages 4, 5, 6, 8, and 11. These norms were based upon the examination of over 4,000 suspected mentally defective immigrants. The Knox Cube Forward (KCF) was part of the Army Performance Scale used during World War I (Yerkes, 1921) for the examination of foreign and illiterate soldiers. Arthur (1925) made the KCF an integral part of her original scale and its revision (Arthur, 1947). Babcock (1952) found the test of great value in the measurement of efficiency of mental functioning. The writer (Levinson, 1956) revised the administration of Knox Cubes by introducing the tapping of the series backwards (KCB). He published norms based upon 75 cases of children ranging in age from four years, four months, to nine years, seven months, with tentative mental ages from four years, nine months, to seven years, three months. (It may be of interest to other investigators that when the writer attempted to teach graduate students the technique of administering the KCB, he noted that administration of the test required certain visual motor attention abilities which not every examiner possessed.)

TESTING PROCEDURE

At the beginning of the testing session, after rapport was established with the aged man, KCF and KCB were administered, followed by WAIS. At the end of the testing session, KCF and KCB were readministered. The score is the average number of correct responses on both the first and second administrations.

Subjects

Our subjects consisted of 105 males ranging from 60 to 84 years of age. The mean age was 68.6 with an SD of 4.4. These men were attending day centers for aged men maintained by the New York City Department of Welfare. They were normal ambulant men who lived in their own homes and were maintaining themselves either on their own savings or on public assistance.

The attitudes of these men to the Knox Cubes varied. Some liked the test; others felt it was childish and beneath their dignity.

RESULTS

Table 1 presents the means, SDs, and ranges of WAIS and Knox Cube scores. The mean KCF score is equal to an MA of 9.0 years (Arthur, 1947), and the mean KCB score is equal to an MA of 7.3 years (Levinson, 1956). There is thus a relative decline of KCB scores as compared with KCF scores. Since in old age these tests may measure other functions than in childhood, the comparison does not necessarily imply decline of intelligence.

Table 2 presents KCF and KCB correlations with other data. It should be noted that both KCF and KCB have a higher correlation with WAIS Verbal than WAIS Performance; furthermore, that KCB scores decline more markedly with age than KCF. Decline in ability with age is also true for the WAIS, but the de-

* The writer wishes to acknowledge the assistance of Mrs. Madelaine Greenberg, who assisted in preparing the tables for this manuscript.

cline has been allowed for in the credits given in the scaled scores (Wechsler, 1955).

Table 3 presents tentative percentiles for the age groups 60-69 and 70-79 for KCF and KCB. As can be noted from the table, there is a gradual decline in scores with age. For example, a man 60-69 years of age who secures a KCF score of 9 has surpassed 37 per cent of his contemporaries. A man aged 70-79 who achieves the same score of 9 has surpassed 51 per cent of his contemporaries. This is similar to the effect of aging noted on other performance tests. At every age, the subjects secure a higher score on KCF than KCB.

DISCUSSION

Various researchers have felt that KCF measures "concentration of attention to a continuously varying task" (Pintner, 1915), or "attention span" (Arthur, 1947), or visual memory (Kent, 1950), or attention and memory (Watson, 1951). The writer has indicated elsewhere that he felt that KCB measures attention, visual imagery and visual motor coordination (Levinson, 1956). Inasmuch as these abilities seem to decline with physical aging, there is a corresponding decrease with age in Knox scores. There is further a general lowering of KCB as compared with KCF scores. This differential change in the Knox test with age is possibly due to the fact that aged men are no longer interested in the test or that they lack visual motor coordination or visual imagery. It is to be remembered that the aged may also be penalized on the test because of their increased movement and reaction time. Deficiencies which may not matter too much to the aged individual are thus exaggerated in the test scores. These differences, however, may be of importance to the clinician. Furthermore, it appears that in certain cases differential impairment of ability may be indicated by a discrepancy between KCF and KCB scores. Thus great disparity in scores between KCB and KCF may indicate attention disturbance, organic impairment, or both. The writer feels that while KCF and KCB may be used as supplementary tests of intelligence, they cannot substitute for an individual test of mental ability. The Knox tests, however, may possibly be used as supplementary tests of mental deterioration in old age.

TABLE 1. MEANS, STANDARD DEVIATIONS AND RANGES OF WAIS AND KNOX SCALE SCORES (N = 105).

	Mean	SD	Range
WAIS Full (IQ)	99.9	15.20	73-159
WAIS Verbal (IQ)	103.3	13.83	71-157
WAIS Performance (IQ)	96.8	13.64	63-161
Knox Cubes Forward (Raw score)	9.8	1.86	3-17
Knox Cubes Backward (Raw score)	6.2	1.82	2-17

TABLE 2. KCF AND KCB CORRELATIONS WITH OTHER DATA (N = 105).

	KCF	KCB
WAIS Full	.46	.43
WAIS Verbal	.53	.51
WAIS Performance	.44	.46
Knox Cubes Forward		.76
Chronological Age	—.27	—.57

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TABLE 3. TENTATIVE PERCENTILES FOR KCF AND KCB (N = 100).[a]

Score	Knox Cubes Forward		Knox Cubes Backward	
	Age Group 60-69 (N = 61)	Age Group 70-79 (N = 39)	Age Group 60-69 (N = 61)	Age Group 70-79 (N = 39)
17	99	—	99	—
16	92	—	97	—
15	—	—	—	—
14	87	—	95	—
13	83	99	89	—
12	72	97	—	99
11	62	92	85	—
10	53	74	80	97
9	37	51	77	90
8	22	41	70	—
7	17	21	62	82
6	—	5	52	79
5	10	3	36	69
4	5	—	25	56
3	2	—	10	23
2	—	—	3	8

NOTE.—The table is to be read as follows: A man in the age group 60-69 whose raw score on KCF was 17 surpassed 99 per cent of his age group.

[a] Scores of five men over 80 years of age not included.

BOOK REVIEWS

Proceedings of the Seminar on the Aging, Aspen, Colorado. Vol. 1. *Toward Better Understanding of the Aging.* Vol. 2. *Social Work Education for Better Services to the Aging.* New York: Council on Social Work Education, 1959. Each volume $2.00. (paper)

These two volumes are based on a seminar held at Aspen, Colorado, September 8-13, 1958, sponsored jointly by the Council on Social Work Education and the National Committee on the Aging, and financed by a grant from the Ford Foundation. Social work educators and practitioners convened for study of "problems contributing to and underlying the critical shortage of qualified social workers in services for old people." Reflected in the seminar program was the *a priori* assumption that social work educators are not fully cognizant of gerontological knowledge and have not successfully incorporated the requisite knowledge, attitudes, and skills into the graduate curriculum.

Volume I presents papers dealing with background knowledge on aging, beginning with one by Leo W. Simmons which, despite the familiarity of its content to all who have read his work, deserves repetition. The seminar could well have been specifically organized around the five basic interests that Simmons attributes to aging persons: life, rest, participation, prerogatives, and an easy and honorable release. One wonders whether the satisfaction of these needs will not involve more basic and imaginative changes in cultural values than are discussed in these two volumes. A conference addressed to implementation of Simmons' challenge that we create a "brave, new climate in which to grow older" would indeed be an exciting event.

Two articles, each by physicians, present a review of the physical and emotional functioning of older people, followed by social work practitioners' analyses of the implications for social work. An excellent review by Ethel Shanas presents the major findings of investigations into the social functioning of older people, and concludes that "the needs of older people are the needs of all people: economic security, something to do, a place to live, and a sense of physical and emotional well being." Comparison of these with Simmons' list, the latter based on studies of primitive cultures, is interesting. Current research apparently has little light to shed on two basic wishes—those for prerogatives and easy and honorable death.

Ollie A. Randall, discussing the implications for social workers of the research surveyed by Shanas, rightly advises caution in drawing inferences from the conclusion that the needs of old people are no different from those of young people. Although the categories of need may be the same, the quality of these needs may be different. Randall finds reassurance in the documentation of observations based on practice, but calls for additional evidence in the case of research findings that are inconsistent with personal experience. This leads to the reviewer's hypothesis, as disturbing as it is not profound, that the receptivity of social workers to research, long a matter of concern, is directly proportional to the degree to which facts fit theories.

Volume II deals with the role of schools of social work in preparing social workers for work in the field of the aging. Social work educators, having achieved unanimity in rejecting the view that graduate education should prepare workers for particular fields of practice, now are enjoined to prepare workers for particular "areas of concern." Volume II is addressed to the dilemma of how to meet the legitimate needs of practice without damage to the desired generic character of the two-year curriculum. Some papers describe welfare needs and services to the aging in group work and in community organization, and some papers describe the content on aging in certain areas of the curriculum. No definitive answer is given to the dilemma. As Grace White points out in her summary, the "knowledge, skills, and attitudes requisite to competent practice with and on behalf of the agency have not yet been identified." When these are identified, there will still remain the problem of how generic the graduate program can be before one teaches common concepts that have been abstracted to the point of meaninglessness, and how specific the curriculum can be before graduate education becomes vocational training. Miss White's remarks concluded the seminar on an eminently sensible note; namely, what should be the goal of the master's program? The next conference might well start with that question. When practitioners and educators share a common orientation on that point, they will have a single criterion regarding the place of special content in the social work curriculum.

ARTHUR S. ROBINS
Professor of Social Work
University of Missouri

The Nature of Retirement. By ELON H. MOORE, edited by GORDON F. STREIB. New York: The Macmillan Co., 1959. Pp. xvi + 217. $4.50.

This book has been published posthumously, with the final editorial work done by Gordon F. Streib. Professor Elon Moore of the University of Oregon came to the study of gerontology at the close of his career, and did not attempt an ambitious "scientific" study. Rather, he collected through interviews and questionnaires the experiences of almost a thousand persons, and used this material to illustrate his own conclusions about retirement.

The book analyzes retirement primarily from the point of view of middle-class people, and advises such people as to how they can live satisfactorily in retirement. Like most American writers, Professor Moore favors a moderately active effort to secure compensatory roles and activities for the loss of the work role.

The book reads well, and is worth recommending to people who want to think about and plan for their retirement. (Eds.)

Social Security Programs Throughout the World: 1958. By the U. S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE. Washington, D. C.: U. S. Government Printing Office, 1958. Pp. xxv + 93. $1.00.

This report presents a summary of the major provisions of existing social security programs in all nations

of the world in chart form under the following divisions: 1) old age, invalidity, and survivors insurance and related programs; 2) health and maternity insurance and related programs; 3) unemployment insurance and related programs; 4) family allowance programs; and 5) work-injuries and related programs. Legislative changes are included down to the early part of 1958. (Eds.)

Aging and Social Health in the United States and Europe. Compiled and edited by CLARK TIBBITTS. Ann Arbor: Published and Distributed for the Social Science Research Committee, International Gerontological Association, by the Division of Gerontology, University of Michigan, 1959. Pp. vii + 186.

This is the report of an international seminar held in Merano, Italy, in 1957, just prior to the meetings of the Fourth International Gerontological Congress. The publication includes introductory statements by Clark Tibbitts and Ernest Burgess, explaining the history of the Social Science Research Committee and the implications of the term "social health"; and at the end, there is a brief statement of proposals for cross-cultural studies. The body of the report is in sixteen papers presented by individual participants in the Seminar. Four deal with employment and income (by Brian Abel-Smith, England, Wilbur Cohen and Seymour Wolfbein, U. S. A., and Pierre Naville, France); four with health and well-being (by Robert van Zonneveld, The Netherlands, Halbert Dunn and Robert Kleemeier, U. S. A., and Ugo Cavalieri, Italy); and eight with family relationships and housing (by Ernest Burgess, Wilma Donahue and E. Everett Ashley, Richard Williams, and Louis Kuplan, U. S. A., Peter Townsend, F. Le Gros Clark and W. A. Sanderson, England, Jean-René Treanton, France, and Angelo Pagani, Italy).

The papers vary in scope and quality. As a group, the four that deal with economic aspects are the most substantive and represent relatively major contributions. (Eds.)

BOOKS RECEIVED

BEYER, GLENN H. *Housing and Personal Values.* (Memoir 364, Cornell University Agricultural Experiment Station.) Ithaca, New York: New York State College of Home Economics, 1959. Pp. 43. free.

CARPENTER, NILES. *Programs for Older People in Great Britain.* (Monographs in Sociology No. 7.) The University of Buffalo Studies, Vol. 24, No. 4, June, 1959. Pp. 287-363. $1.25. (paper)

FAUNCE, FRANCES AVERY. *Those Later Years.* New York: Thomas Y. Crowell Co., 1959. Pp. 177. $3.50.

FEDERATION OF PROTESTANT WELFARE AGENCIES, INC. *Manual of Forms and Procedures for Use by Homes for the Aged.* 1. *Guide on Personnel Policies and Practices.* 2. *Medical and Nursing Services.* 3. *Menumaker for Homes for the Aged.* New York: The Federation, Division on Aging, 251 Fourth Avenue. Each section published separately. 50 cents each. (paper)

INTERNATIONAL ASSOCIATION OF GERONTOLOGY, SOCIAL SCIENCE RESEARCH COMMITTEE. *Aging and Social Health in the United States and Europe: Report of an International Seminar Held at Merano, Italy, July 9-13, 1957.* Ann Arbor: Division of Gerontology, University of Michigan, 1959. Pp. vii + 186. (paper)

MORE, ELON H. *The Nature of Retirement.* New York: The Macmillan Co., 1959. Pp. xvi + 217. $4.50.

Seminar on the Aging, Aspen, Colorado, September 8-13, 1958. Vo. 1. *Toward Better Understanding of the Aging.* Vol. 2. *Social Work Education Services to the Aging.* New York: Council on Social Work Education, 345 East 46th Street, 1959. Each volume $2.00. (paper)

TRINITY EPISCOPAL CHURCH, WASHINGTON, D. C. *Community Resources in the Metropolitan Washington Area, With Particular Reference to the Aging: Selected Notes from an Institute on Community Resources.* Washington, D. C.: Department of Social Relations, Diocese of Washington, 1702 Rhode Island Avenue, 1959. Pp. 16. 50 cents. (paper)

U. S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE. *Social Security Programs Throughout the World: 1958.* Washington, D. C.: U. S. Govt. Print. Off., 1958. Pp. xxv + 93. $1.00. (paper)

WOLFF, KURT. *The Biological, Sociological and Psychological Aspects of Aging.* Springfield (Ill.): Charles C Thomas, 1959. Pp. 95. $3.75.

WOLTERECK, HEINZ. *A New Life in Your Later Years.* New York: Dial Press, 1959. Pp. xv + 194. $3.75.

JOURNAL OF GERONTOLOGY

VOLUME 15, NUMBER 1

JANUARY, 1960

Section C

Organization Section
Index to Current Periodical Literature

VOLUME 15, SECTION C JANUARY, 1960 NUMBER 1

ORGANIZATION SECTION

GERONTOLOGICAL SOCIETY, INC. COUNCIL FOR 1960

President	Nathan W. Shock (Baltimore)	Past President	Louis Kuplan (Sacramento)
President-Elect	Joseph T. Freeman (Philadelphia)	Treasurer	John E. Kirk (St. Louis)
	Secretary	Robert W. Kleemeier (St. Louis)	

	to serve through
Biological Sciences	
Norman M. Sulkin (Winston-Salem)	1960
J. Murray Steele (New York)	1962
Clinical Medicine	
Leo Gitman (Brooklyn)	1960
Herman T. Blumenthal (St. Louis)	1962
Psychological and Social Sciences	
Ethel Shanas (Chicago)	1960
Irving L. Webber (St. Petersburg)	1962
Social Welfare	
Jerome Kaplan (Mansfield, Ohio)	1960
Jacob G. Gold (Chicago)	1962
General Membership Division	
Helen Zollinger (Portland, Oregon)	1960
Herbert Shore (Dallas)	1961
Affiliate Organization Division	
Harold E. Jones (Berkeley)	1960
Chairman, Research and Fellowships Committee	
Robert J. Havighurst (Chicago)	1961

PAST PRESIDENTS OF THE SOCIETY

William deB. MacNider	1945
Roy G. Hoskins	1946
Lawrence K. Frank	1947
Joseph C. Aub	1948
Clive M. McCay	1949
C. J. Van Slyke	1950
Robert A. Moore	1951
Ernest W. Burgess	1952
E. Vincent Cowdry	1953
Anton J. Carlson	1954
Ollie Randall	1955
William B. Kountz	1956
Robert J. Havighurst	1957
Albert I. Lansing	1958
Louis Kuplan	1959

Representative on the Governing Body of the International Association of Gerontology
Robert J. Havighurst 1958-1960

Representative to the American Association for the Advancement of Science
Nathan W. Shock 1959-1961

SUMMARY OF THE MINUTES OF THE FOURTEENTH ANNUAL MEETING OF THE COUNCIL AND MEMBERS OF THE CORPORATION OF GERONTOLOGICAL SOCIETY INC.

The meeting was called to order by President Louis Kuplan at 9:06 a. m., November 11, 1959, at the Statler-Hilton Hotel, Detroit, Michigan. Members of the Council present were Nathan W. Shock, John Esben Kirk, Norman M. Sulkin, Warren Andrew, Robert T. Monroe, Leo Gitman, Ben L. Grossman, Herbert Shore, Harold E. Jones, and Robert W. Kleemeier. Ethel Shanas and Robert J. Havighurst, although not present at the opening of the meeting, were also in attendance. Jerome Kaplan did not attend the sessions on November 11, but was present on November 13. Absent were Helen Zollinger and Gordon F. Streib.

Minutes of the Thirteenth Annual Meeting of the Council were approved as published in the January, 1959, issue of the Journal of Gerontology.

Mr. Kuplan announced the appointment of Mr. Grossman as Chairman of the Finance Committee. In his report on his activities as President during the preceding year, Mr. Kuplan stated that the Gerontological Society had been officialy represented at the meetings of 6 national organizations interested in gerontology.

Mr. Kuplan discussed at length the replies he had received to a letter of inquiry sent to a sample of members of the Society. The purpose of this letter was to obtain the opinion of the selected sample on a number of issues concerning the aims and purposes of the Society which Mr. Kuplan thought had bearing on its future course of action. His report stimulated discussion and resulted in a proposal, which was carried, that the incoming President appoint a Policy and Planning Com-

mittee to hold several meetings during the year to discuss matters pertaining to the general welfare of the organization, and that a sum not to exceed $750.00 be appropriated for the expenses of this Committee.

In addition the Council decided that senior members of the Fellowship Review Committee should review the basic requirements for granting Fellowship status in their Sections; to reevaluate and if necessary rewrite the requirements and report their findings at the next annual meeting of the Council.

With reference to the matter of public relations brought up in the President's report, Mr. Shore's motion that the Society, through its Public Relations Committee, create an exhibit designed to interpret its aims and purposes was carried. It was hoped that this exhibit could be placed on view at various regional and national meetings and that therefore it be dignified in character and free of slogans. The desire was further expressed that one of our affiliate organizations be asked to undertake this project at no cost to the Gerontological Society.

The matter of encouraging the establishing of local chapters of the Gerontological Society and the affiliation of interested local and regional gerontological organizations was discussed. This resulted in the following motion presented by Dr. Shock: that a committee be appointed composed of members of the Society representing various regions of the country with the aim of securing additional affiliate organizations and preferably local chapters for the Gerontological Society, and that a sum of $500.00 be appropriated to cover the expenses of this Committee. The motion was passed.

With reference to the Editorial Board, it was noted that this body is referred to in the bylaws as the Publications Committee. The consensus of the Council was that in the future it should be so designated by this official title. Further action with reference to publication resulted in the appointment of Dr. Robert W. Kleemeier as Chairman *pro tem* of the Publications Committee and the stipulation that a representative from the Sections on Biological Sciences and Social Welfare be placed on the Committee.

The possibility of establishing a new journal designed to give the membership of the Society broader opportunities for publication than now exist was placed in the hands of the Policy and Planning Committee for their consideration and recommendation. It was emphasized that no change in the present research orientation of the Journal of Gerontology be considered.

The order of presidential rotation through the various professional sections was discussed at length. It was brought out that last year the Section on Clinical Medicine had relinquished its position to the Section on Biological Sciences with the understanding that the nomination for the presidency of the Society would this year be from the membership of the Section on Clinical Medicine rather than the Section on Psychological and Social Sciences as otherwise would have been the case. This action was recommended by the Nominations Committee and submitted to the Council at its 1958 meeting. Since this action had been accepted by the Council it was therefore considered binding.

Dr. Kirk submitted the Treasurer's report in which he stated that the Society is in a reasonably good financial position, with the current expenditures being held within the limits of the Society's income.

With reference to the proposed budget, the following action was taken: $75.00 was allotted to each of the 4 Professional Sections and to the General Division for the conduct of their business; an increase of $900.00 a year was approved for the salary of the Administrative Secretary; the part-time position of clerk-typist was established on a yearly basis at the rate of $2.00 per hour with a maximum of $2,210.00 per year. A one-week vacation with pay was approved for the latter position, and in addition Social Security payments were approved for permanent employees of the Society. The above salary provisions are to become effective January 1, 1960. An increase of $500.00 was granted for expenses associated with the editing of Section B of the Journal of Gerontology for the year 1960.

A $100.00 advance allotment was made to the Local Arrangements Committee for the 1961 annual scientific meeting, with the provision that this Committee be instructed to raise needed funds for the satisfactory completion of their work from registration fees and other outside sources. It was further moved and passed that the Program Committee expenses for the 1959 annual meeting as submitted by Dr. Donahue be paid out of unused 1959 Professional Section funds.

The meeting was recessed at 12:55 p. m. and resumed at 2:10 p. m.

The Secretary submitted his report on membership of the Society, stating that there is a total of 2,199 members, of whom 1,208 are Fellows and members of the Professional Division of the Society. This is an increase of 365 members over 1958.

In view of the discussion of membership requirements of the various Sections it was moved, seconded, and passed that the list of applicants for membership in the 4 Professional Sections be admitted to General Membership in the Society with the understanding that the Secretary and the Membership Committee would work out the assignment to the appropriate Professional Sections.

In his report as Editor-in-Chief of the Journal of Gerontology, Dr. Kirk indicated that the subscription list had increased by 187 subscriptions to a total of 2,330 subscriptions as of October 1, 1959. Subscriptions to the Newsletter totaled 3,101. He commended especially the fine work of Drs. Havighurst and Neugarten in the editorship of Section B.

Mr. Kuplan read the report of Dr. Oscar Kaplan, Editor of the Newsletter, in which the suggestion was made that the possibility of expanding the present Newsletter or the establishment of a new journal be considered.

Dr. Gitman, Chairman of the Committee on Exhibits, stated that the Committee experienced difficulty in securing appropriate and acceptable commercial exhibits and recommended that this function be dropped after the 1960 joint meeting of the International Association of Gerontology and the Gerontological Society.

Mr. Shore asked for a clarification of the Membership Committee's functions, and it was the consensus of the Council that pending the recommendations of the Policy and Planning Committee, the Membership Committee should try, 1) to increase the number of professional memberships in the Society, 2) to increase the general

memberships of the Society among lay people actively interested in the fields of aging, e.g., delegates to the White House Conference, community leaders in this area, etc.

Mr. Grossman reported on the findings of the Nominations Committee. Its recommendations were as follows: Treasurer, John Esben Kirk; Secretary, Robert W. Kleemeier; representatives from the professional sections, Biological Sciences, J. Murray Steele; Clinical Medicine, Herman T. Blumenthal; Psychological and Social Sciences, Irving L. Webber; Social Welfare, Jacob Gold. In view of the lack of clarification on the order of rotation of the Presidency discussed above, the Nominations Committee was unable to offer a name for the president-elect at this time. The Council, therefore, accepted the report of the Nominations Committee and proceeded immediately to secure the nomination of the president-elect. This action resulted in the nomination of Dr. Joseph T. Freeman.

The report of the Local Arrangements Committee recommending that the 1961 annual scientific meeting be held at the Penn Sheraton Hotel in Pittsburgh, Pennsylvania, on November 10 and 11 was submitted. Since the Committee had made reservations at the hotel for only 2 days, the Secretary was instructed to write the Chairman of the Local Arrangements Committee, Dr. Thomas Moran, that 2½ days would be required to complete the program for the annual meeting, and that commitment should be made with the hotel for this additional half day.

At this point Mr. Popkin, the representative of the Michigan Gerontological Society, was invited into the meeting to read a statement from the Michigan Society concerning affiliation with the Gerontological Society.

Following the report of Dr. Gertman, Chairman of the Place of Meeting Committee, the following action on the place of future annual meetings was taken: 1962, Miami Beach; 1963, Boston; and 1964, Dallas, provided that no restrictions would be made by the hotels in the housing of members. The incoming President was given the authority to appoint all necessary committees for local and program arrangements for all annual meetings up to and including 1964.

The report of the committee on history was accepted as submitted by Dr. Irving L. Webber, as was the report of the Committee on Research Grants and Fellowships as submitted by Dr. R. Havighurst. Reports of sub-committees of the latter committee, as submitted by Dr. Albert I. Lansing and Dr. R. Kleemeier were also accepted.

Dr. Shock, representative to the American Association for the Advancement of Science, submitted his report of activities. It is noteworthy that the Gerontological Society is co-sponsoring a symposium on aging with Section N (Medical Sciences) of the AAAS at its 1959 meeting. Dr. Shock is Chairman of Section N.

It was moved by Dr. Shock and accepted by the Council that the dues structure of the Gerontological Society remain unchanged.

Mr. Kuplan reported on organizational matters and plans concerning the Fifth Congress of the International Association of Gerontology to be held in San Francisco, August 7-12, 1960.

It was moved, seconded, and passed, that the charters of the Western Gerontological Society, the Florida Council on Aging, and the Texas Society on Aging be renewed.

The meeting was recessed at 5:00 p. m. and reconvened at 1:15 p. m. November 13, with Mr. Kuplan, Dr. Shock, Dr. Andrew, Dr. Sulkin, Dr. Kirk, Dr. Monroe, Dr. Gitman, Dr. Shanas, Mr. Kaplan, Mr. Shore, Dr. Jones, Dr. Havighurst, and Dr. Kleemeier present. Dr. Tibbitts, invited to give a report on proposed changes in the bylaws of the International Association of Gerontology, was present during the discussion of this topic.

After considerable discussion, the suggested changes in the bylaws of the International Association of Gerontology, which had been previously submitted for inspection of the Council were approved, with the recommendation that consideration of the admission of other types of organizations not now eligible should not be excluded.

Mr. Kuplan reported that the Chairmanship of the Public Relations Committee had been accepted by Mr. Jerome Kaplan, who has agreed to submit a written report on plans and proposed activities by January 1, 1960.

A suggested design for a seal of the Gerontological Society, prepared by Dr. Joseph Falzone at the request of the Council, was presented. Much interest was expressed in his design, and a Committee composed of Dr. Shock, Dr. Gitman, and Mr. Kaplan was appointed to explore the matter further.

With reference to the matter of health insurance for members of the Society, it was decided that investigation of its feasibility as suggested by Dr. Abelson be tabled pending the completion of the report of the Policy and Planning Committee.

Following the reports of the Business Meeting of the 4 Professional Sections and the General Membership Division the meeting was adjourned at 3:25 p. m.

ROBERT W. KLEEMEIER, Secretary

SUMMARY OF THE MINUTES OF THE TWELFTH ANNUAL BUSINESS MEETING OF GERONTOLOGICAL SOCIETY INC.

In the absence of the President, Mr. Louis Kuplan, the meeting was called to order by the Secretary, Dr. Robert W. Kleemeier, at 1:20 p. m., November 14, 1959, in the Michigan Room of the Statler-Hilton Hotel, Detroit, Michigan. Approximately 70 members were present.

The Minutes of the Eleventh Annual Business Meeting were approved, and the actions and recommendations of the Council (see above Minutes) were reported by the Secretary. The report of the Corporation for 1958 was made available to the members of the Society for their inspection.

Dr. Kleemeier then reported briefly on the action taken by the Council at its meeting.

The proposed change in Article III, Section 2c, of the bylaws regarding election to membership, which had

been previously circulated, was approved. This Article now reads as follows:

Action on applications for membership shall be taken by the Secretary on the basis of criteria which he and the Membership Committee believe are adequate. The criteria may differ for membership in the Professional Sections and in the General Member Division. It is understood that all applicants of good character and definite interest in the field of gerontology shall be admitted to the General Member Division. Dues of Members shall be fixed in accordance with Article XI of these Bylaws.

Mr. Jerome Kaplan, in the absence of Mr. Ben Grossman, Chairman of the Nominating Committee, presented the slate of officers recommended by the Council. These were: President-elect, Dr. Joseph T. Freeman; Secretary, Dr. Robert W. Kleemeier; Treasurer, Dr. John Esben Kirk; Council Representative for Section on Biological Sciences, Dr. J. Murray Steele; Section on Clinical Medicine, Dr. Herman T. Blumenthal; Section on Psychological and Social Sciences, Dr. Irving L. Webber; Section on Social Welfare, Mr. Jacob Gold. There were no nominations from the floor, and the slate was elected by unanimous vote.

On a motion by Dr. Robert Monroe, a vote of commendation was accorded to Dr. Wilma Donahue, Program Chairman, to Dr. A. H. Price, Chairman of the Local Arrangements Committee, and to the members of their committees.

The meeting was adjourned at 1:45 p. m.

ROBERT W. KLEEMEIER, Secretary

APPLICATIONS FOR FELLOWSHIP STATUS IN GERONTOLOGICAL SOCIETY, INC. APPROVED IN 1959

Section on Biological Sciences

Eli D. Goldsmith, New York
M. Mason Guest, Galveston
George Miroff, Grand Forks
Morris H. Ross, Newark
Edgar Anthony Tonna, New York
A. Kurt Weiss, Coral Gables

Section on Clinical Medicine

Lee James Cordrey, Tampa
Elias D. Padernacht, Brooklyn
B. H. Webster, Nashville

Section on Psychological and Social Sciences

R. O. Beckman, Hialeah
Martin J. Forman, Taipei
Carter C. Osterbind, Gainesville

Social Welfare

Jack Esman, Memphis
Margaret Harwick Jacks, Jacksonville
Betty Jane Rank, Seattle

OFFICERS OF AFFILIATE ORGANIZATIONS AND LOCAL CHAPTERS

Western Gerontological Society

Council Members

Harold E. Jones, President (Berkeley)
John Beeston, President-Elect (Los Angeles)
Mrs. A. M. G. Russell, Secretary-Treasurer (Menlo Park)

Biological Sciences
Hardin Jones, Berkeley
Harry Sobel, Los Angeles

Clinical Medicine
Lincoln Cromwell, Sna Diego
Lester Breslow, Berkeley

Social Welfare
Beverly André, Orange (Calif.)
Louis Kuplan, Sacramento

General Membership
Mercia Kahn, San Francisco
Selmer Wake, Santa Barbara

Psychological and Social Sciences
Margaret Gordon, Berkeley
Oscar Kaplan, San Diego

Florida Council on Aging

Margaret Jacks, President (Jacksonville)
Henry Richards, President-Elect (Tallahassee)
Percy J. Feany First Vice-President (St. Petersburg)
Louis Amato, Vice-President (Fort Lauderdale)
Louise Davis, Vice-President (Jacksonville)
Carter Osterbind, Vice-President (Gainesville)
S. E. Hand, Vice-President (Tallahassee)
L. L. Parks, Secretary-Treasurer (Jacksonville)
Irving L. Webber, Past President (St. Petersburg)

Texas Society on Aging

EXECUTIVE COMMITTEE

Ernest W. Keil, President (Temple)
Hiram J. Friedsam, President-Elect (Denton)
Ozro T. Woods, Vice-President (Dallas)
Herbert Shore, Past President (Dallas)
Mrs. William B. Ruggles, Secretary-Treasurer (Dallas)
Wendell Gingrich (Dallas)
W. R. Ransone (Dallas)
Mrs. Nina Spoonemore (Pampa)
Mrs. Edith DeBusk (Dallas)
Louise Evans (Amarillo)

FIFTH CONGRESS OF THE INTERNATIONAL ASSOCIATION OF GERONTOLOGY

PROGRAMS IN BIOLOGICAL SCIENCES AND CLINICAL MEDICINE

Dr. Nathan W. Shock, Chairman of the American Research Committee in Biological Sciences, and Dr. Herman T. Blumenthal, Chairman of the American Research Committee in Clinical Medicine, have announced the format of the program for their Sections of the Congress. The program has been planned to present these two sections in an integrated form. Thus there will be two symposia, one dealing with the basic biology of cell growth and aging and their relation to cancer, and the second dealing with the basic biology and aging of connective tissue and their relation to human disease involving connective tissue structures.

There will be 6 sessions in each of the Biological Sciences and Clinical Medicine sections. The fields to be covered in biology are (1) A-Genetics, B-Comparative Longevity, (2) Body Composition, (3) Regulatory Systems, (4) Environmental Factors, (5) A-Cell Structure, B-Cell Physiology, and (6) Connective Tissue. The 6 fields to be covered in Clinical Medicine are (1) Endocrinological and Neurological Regulatory Systems, (2) Psychiatry, (3) Respiratory System, (4) Skeletal System, (5) Cardiovascular-Renal Systems, and (6) Physician's Responsibility in an Aging Society.

Each symposium and session will be jointly conducted by an American and a foreign Chairman, who will also present a general summary of the subject of the session as a final presentation. All participants in the symposia will be invited and will speak on specific topics. The sessions will contain both invited and contributed papers.

PROGRAM IN PSYCHOLOGICAL AND SOCIAL SCIENCES

Dr. Ernest W. Burgess, Chairman of the American Research Committee in Psychological and Social Sciences, has announced that the program for the Section will be organized around 6 major topics:

1. Economics: Employment, Retirement, and Income. Dr. Seymour Wolfbein, U. S. Department of Labor, and Mr. Henning Friis, Denmark, organizers.

2. Psychologoy of Aging: Experimental Studies. Dr. James E. Birren, National Institute of Mental Health, and Dr. Alan T. Welford, England, organizers.

3. Personality Theory, Attitudes, Roles, and Adjustments. Professor Bernice Neugarten, The University of Chicago, and Dr. Jean-René Treanton, France, organizers.

4. Housing, Family, and Social Relationships. Dr. Wilma Donahue, The University of Michigan, and Mr. Peter Townsend, England, organizers.

5. Mental Health and Rehabilitation. Dr. Richard H. Williams, National Institute of Mental Health, organizer.

6. Population and Social Organization. Professor Leonard Z. Breen, Purdue University, and Dr. Pierre Naville, organizers.

Each of the sessions will feature both invited and contributed papers, all of which will necessarily be short reports of research.

PROGRAM IN SOCIAL WELFARE

Mr. Louis Kuplan, Chairman of the American Research Committee in Social Welfare, has announced a symposium, An Evaluation of European and American Social Welfare Programs for Older People.

The program for the sessions is tentatively planned around the following topics: (1) Case work Services, (2) Housing, (3) Institutional Care, (4) Retirement Planning and Counseling, (5) Leisure Time Activities, (6) Social Aspects of Medicine, (7) Income Maintenance, (8) Community Organization, and (9) Public Health Programs. In the event that the final program includes all 9 subjects, three of the sessions will be run concurrently with other sessions.

INDEX TO CURRENT PERIODICAL LITERATURE

NATHAN W. SHOCK
Gerontology Branch
National Heart Institute
National Institutes of Health

THE subject categories are those in *A Classified Bibliography of Gerontology and Geriatrics* by Nathan W. Shock published by Stanford University Press, Stanford, California (1951). Only major headings are used and the Roman numerals correspond to those given in the bibliography. In so far as possible, references are classified according to organ systems. Thus, most of the material on Geriatrics will be found under the organ system involved in the disease. Cross references are indicated by number at the end of each section. When available, abstract references are given. (*B. A.—Biological Abstracts, P. A.—Psychological Abstracts,* and *P. I.—Population Index*). Abbreviations for journals are those used in *A World List of Scientific Periodicals Published in the years 1900-1933, 2nd Edition.* For journals not listed, abbreviations were devised according to the general rules used in the above source. It is impossible to cover all journals and list all papers concerned with aging and the aged. Authors and publishers are requested to call attention to publications or to send reprints to the Gerontology Branch, Baltimore City Hospitals, Baltimore 24, Maryland. The assistance of the Forest Park Foundation, Peoria, Illinois, in the preparation of these materials is gratefully acknowledged.

GERONTOLOGY

28041. Arnoult, M. D.: The phenomena of aging. *Miss. Doctor, 36:* 269-274, 1959.

28402. Berends, F., C. H. Posthumus, I. V. D. Sluys, and F. A. Deierkauf: The chemical basis of the "ageing process" of DFP-inhibited pseudocholinesterase. *Biochim. et biophys. Acta 34:* 576-578, 1959.

28043. Bortz, E. L., and W. M. Bortz: Major issues of aging. *GP, 20:* 84-95, 1959.

28044. Bugard, P.: Essai de mesure de la résistance et de l'usure organique à l'aide d'une batterie de tests. Application à la fatigue chronique et à la sénescence. *Rev. franç. Géront., 5:* 287-291, 1959.

28045. Gerontological Society, Inc.: Abstracts of papers to be presented and exhibits. (Twelfth annual scientific meeting of Gerontological Society, Inc.). *J. Geront., 14:* 491-515, 1959.

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(ovaries, testis, See Endocrine System)

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